

ACTA OPHTHALMOLOGICA

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Editor

POUL BRÆNDSTRUP KOBENHAVN

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CONGRESSUS XIX OPHTHALMICORUM SEPTENTRIONALIU

XIX MEETING OF NORDIC OPHTHALMOLOGISTS
held in Bergen June 18th to 21st 1969

OFFICIAL TRANSACTIONS

(Edited by *H Aasved* Bergen)

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1970

Acta Ophthalmologica has completed its 1969 volume – larger than ever. It is a gratifying sign of thriving that so many contributors have entrusted their publications to Acta ophthalmologica.

Acta had a precursor in the nineteenth century: Nordisk ophthalmologisk Tidsskrift. Since, however, this periodical was written in the Scandinavian languages, it could not expect any wide circulation, and indeed it ran for only a few years. At that time Scandinavian ophthalmologists had to send their papers for publication to foreign journals, which involved various difficulties. Scandinavian thinking, characteristics and tradition were often lost, more or less, in the adaptation of the publications to the demands of a foreign editorial board. To this very day several renowned Scandinavian ophthalmologists are believed to be English, French or German, because their papers were published in journals of these nationalities.

Acta Ophthalmologica is owned by the ophthalmological societies of the Scandinavian countries, and its editors are appointed by these societies. Quite naturally, Acta Ophthalmologica is therefore primarily a forum for Scandinavian publications, but in the course of time many authors from other countries have found their way to its columns.

Anyone who has tried must admit that it is by no means easy to present one's thoughts in a foreign language. Even with the aid of translators it is difficult to preserve subtle differences and to avoid errors entirely. The editors must still trust in the readers' indulgence, but will make every effort to do better.

The editing of Acta Ophthalmologica has always been characterized by tolerance. Censorship in science is just as unattractive as it is in politics. Whether an author's views coincide with those of the editorial board or with expert opinion is immaterial. Of course the editors must call attention to downright errors or defects, but without rejecting a new idea or an original observation. I

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If a person's publications are to be assessed as a basis for an appointment to a post official or honorary it is naturally of the utmost importance that they be correct and flawless. In an editorial evaluation the main thing is whether a paper brings something of value. In science it is positivity which counts. Fruitful ideas, observations and experiments do not lose their value merely because they are presented in an unsatisfactory way. The editorial board should not play the part of a schoolmaster discouraging the contributors. Even a demand as simple as a given rigid system of listing references may seem almost prohibitive to writers in far away places.

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For the tribute rendered by my co editors by dedicating without my knowledge fascicle 3 to me on occasion of my 70th birthday I want to express my sincere thanks to all contributors and my cordial forgiveness to my friends on the editorial board.

Holger Ehlers
Ex editor

*From the Departments of Ophthalmology and Pathology
Hacettepe University Medical Faculty Ankara Turkey*

HISTOCHEMICAL INVESTIGATIONS ON LIGNEOUS CONJUNCTIVITIS AND A NEW METHOD OF TREATMENT

BY

TANJU FIRAT and BEHÇET TINAZTEPE

Ligneous conjunctivitis is one of the rare forms of membranous conjunctivitis. This chronic recurrent and somewhat peculiar form of conjunctivitis was first described by Lijo Pavia in 1924. Morax (1929) made the first anatomic pathologic investigation and used the term granuloma. In 1935 Borel introduced the term ligneous conjunctivitis. Duke Elder (1965) found about 50 cases in ophthalmic literature.

Ligneous conjunctivitis is rarely unilateral affecting girls more than boys. It causes severe corneal complications which usually end with perforation and quite often the loss of both eyes.

The membrane is hard and may be 1 or 2 mm thick. Haemorrhages occur when removal is attempted and they reform within a few days thicker than before. No specific microorganisms cultivated.

Treatment was ineffective and the etiology was unknown (Duke Elder 1965, Herx et al 1966, Katsourakis and Roussas 1966, Spaeth 1961) till recent publications by François and his co-workers (1966, 1961, 1968) who proposed new etiological ideas and therapeutic possibilities.

François and his co-workers (1966) have demonstrated the existence of mucopolysaccharides in the constitution of the lesions by means of special staining methods and histochemical analyses.

Mucopolysaccharides are colored using specific staining methods and lose this coloring when the specimens are treated with hyaluronidase, acting as a

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Holger Ehlers
Ex editor



Fig 2

Abundant fibrillary material around the islets of epithelioid cells
(Hematoxylin eosin $\times 20$)

4 Alcian blue combined with P A S was used to show acid and neutral polysaccharides. Acid mucopolysaccharides are stained in blue with Alcian blue while they become violet red with P A S. Neutral mucopolysaccharides are also stained with P A S (Fig 3)

5 Hyaluronidase digestion in Alcian blue stained sections produced a palor of the digested part (Fig 4)

6 In hyaluronidase digested sections stained with P A S and Alcian blue the P A S positive material did not disappear entirely while the blue stained acid mucopolysaccharides were completely dissolved (Fig 5)

7 I A S staining was positive and remained so after ptyalin (salivary) digestion and this confirms presence of mucopolysaccharides

8 Fibrin which participates in the membrane formation was stained in blue with phospho tungstic acid hematoxylin (Fig 6)

dissolvent of hyaluronic acid and chondroitin sulphuric acid. Having obtained the same results in all their work *François et al* (1966, 1967, 1968) forwarded the hypothesis of a disturbance of mucopolysaccharides metabolism in connective tissue and tried successfully a new treatment of ligneous conjunctivitis with local application of hyaluronidase in combination with alpha chymotrypsine.

Histochemical and histopathological investigations were carried out on the biopsy material of two cases of ligneous conjunctivitis seen at the Department of Ophthalmology Hacettepe University Medical Faculty, Ankara the second been treated successfully.

Material and Method

Biopsy material was fixed in 10% formalin and paraffin. In different sections various special staining methods were used.

- 1 Hematoxylin eosin staining for general view
- 2 Metachromasie with toluidine blue (Ph 3.5) for acid mucopolysaccharides (hyaluronic acid and chondroitin sulphate)
- 3 Alcian blue (S Gx) for acid mucopolysaccharides
- 4 Alcian blue and P A S for acid and neutral mucopolysaccharides
- 5 Sections stained with Alcian blue were digested with hyaluronidase (150 U solved in 1 cc of serum) and left in room temperature for one hour
- 6 Sections stained with Alcian blue and P A S were digested with hyaluronidase
- 7 P A S staining was also used with and without digestion
- 8 Phospho tungstic acid hematoxylin staining to show the fibrin content of the membrane

Results

1 Sections stained with hematoxylin eosin showed abundant inflammatory cells among membranous tissue, fine fibrillar bundles and epitheloid islets crossing each other or parallel (Fig 1).

2 A dark pink metachromatic appearance was observed in some areas with toluidine blue (Fig 2).

3 Acid mucopolysaccharides were stained by Alcian blue. This dye was preferred as the Reinhardt Abul Haj colloidal technique is more complicated (Mc Manus and Mowry, 1960).

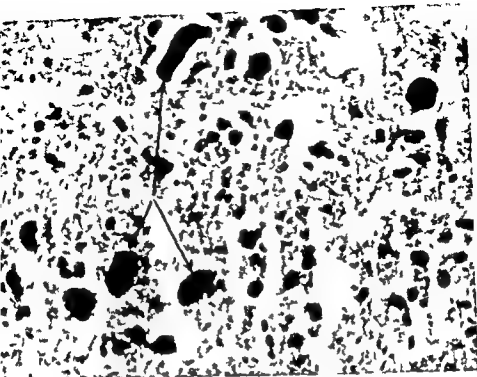


Fig 5

Irregular globules of Alcian blue positive material (indicated by arrows) on the background of P A S positive material showing acid and neutral mucopolysaccharides (Alcian blue + P A S X 63)

condition was more severe in the right eye where it was complicated by a corneal ulcer and iridocyclitis. Bleeding occurred on any attempt to remove the membranes (Fig 10). Laboratory results were all negative except mucopolysaccharide dosage in the urine as the Anthrone method revealed a high level (1157/165 ml) compared with normal of 995/6/165 ml).

At this time the sensational results obtained by François (1967) were published and the histochemical constitution was shown (François et al 1966).

While carrying out histochemical investigations we started the treatment immediately.

We used a 1/10,000 dilution of alpha chymotrypsine and a solution of 35 U hyaluronidase per cc. Two drops of these drugs were instilled in both eyes every hour for two months.

After two weeks the hardness of the membranes was already diminished and it was easier to remove them without bleeding. Seventy days after the beginning of the treatment the membranes had disappeared at the left eye and later at the right eye. The keratitis healed also leaving only a paracentral nebula of the right cornea (Figs 11 & 12).

Drug dosage was gradually decreased to six drops a day and then three drops a day.

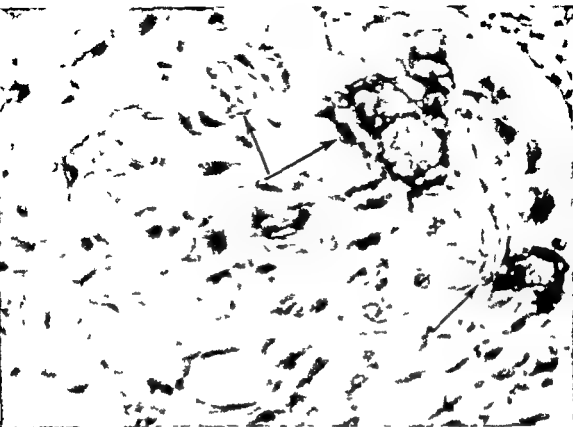


Fig 2

Metachromatic appearance indicated by arrows dark pink coloring among blue stained cells (Toluidine blue $\times 400$)

Case Reports

Case 1 H K a 20 days old female baby showed thick white membranes on upper and lower lids of the right eye with bleeding from the conjunctiva on any attempt to remove them (Fig 7) No treatment was effective The laboratory investigations were negative Four months later the membranes were thicker and the general condition was deteriorated (raised temperature enlarged liver pharyngitis and hypochrom anemia) Group agglutinations for brucella melitensis and salmonella V D R L and Schick test were negative No microorganisms were found in the conjunctival cultures Streptococcus neisseria and pneumococcus were identified from the throat culture

Three months later the left eye was also involved in the same way (Fig 8)

Local and general antibiotics combined with steroids and local antidiabetic serum were ineffective

The child died at the age of two years from pneumonia the conjunctival membranes still present

Case 2 H A a 4 year old boy was seen in April 1968 with a typical leucocytoclastic conjunctivitis Thick membranes were found on both upper and lower lids (Fig 9) The

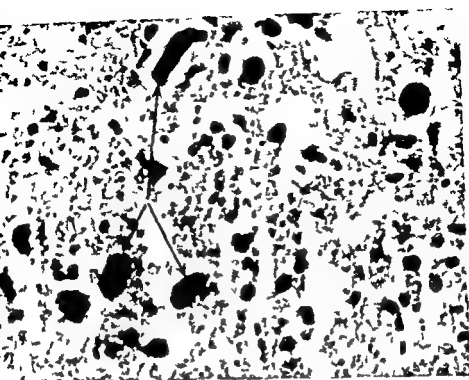


Fig. 9

Irregular globules of Alcian blue positive material (indicated by arrows) on the background of I A S positive material showing acid and neutral mucopolysaccharides (Alcian blue + PAS $\times 15$)

condition was more severe in the right eye where it was complicated by a corneal ulcer and iridocyclitis. Bleeding occurred on any attempt to remove the membranes (Fig. 10). Laboratory results were all negative except mucopolysaccharide dosage in the urine as the Anthrone method revealed a high level (1157/16.5 ml compared with normal of 93 G/16.5 ml).

At this time the sensational results obtained by François (1964) were published and the histochemical constitution was shown (François *et al* 1966).

While carrying out histochemical investigations we started the treatment immediately. We used a 1:10,000 dilution of alpha chymotrypsine and a solution of 55 U hyaluronidase per cc. Two drops of these drugs were instilled in both eyes every hour for two months.

After two weeks the hardness of the membranes was already diminished and it was easier to remove them without bleeding. Seventy days after the beginning of the treatment the membranes had disappeared at the left eye and later at the right eye. The keratitis healed also leaving only a paracentral nebula of the right cornea (Figs. 11 & 12).

Drug dosage was gradually decreased to six drops a day and then three drops a day.

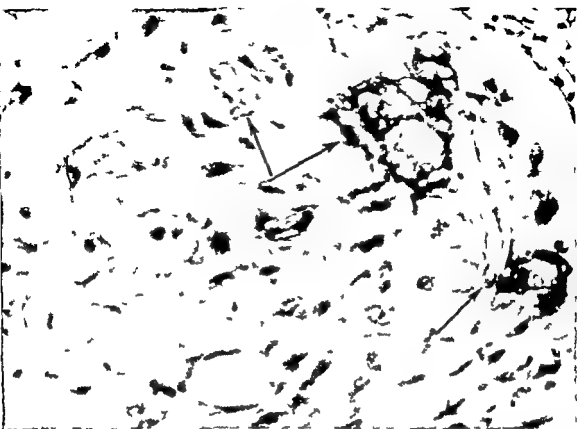


Fig 2

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Case Reports

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Fig 5

Acid mucopolysaccharides are entirely dissolved by hyaluronidase digestion while P & S material is not dissolved (arrows) (Alcian blue + P A S $\times 75$)

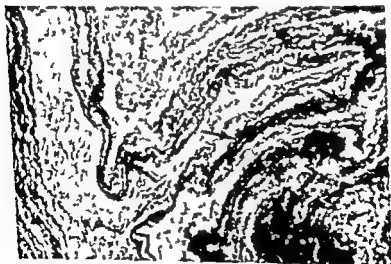


Fig 6

Wave appearance of fine fibrine bands in the ligneous membranes (arrow) (Phosphotungstic acid + hematoxylin, $\times 75$)

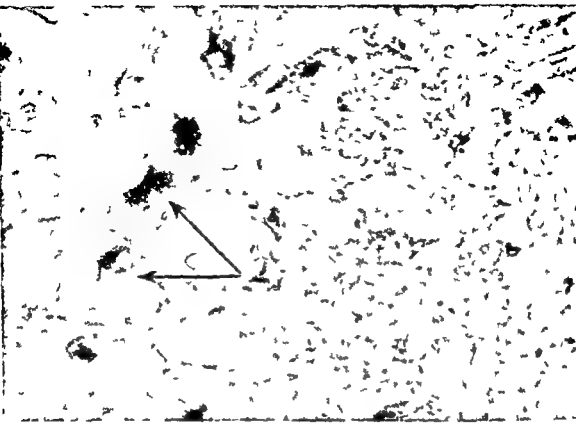


Fig 4

Section after hyaluronidase digestion. The right part of the slide is pale due to digestion proving the presence of acid mucopolysaccharides while the non treated part remains darker (arrows) (Alcian blue $\times 400$)

over a period of three and half months. The patient was seen after 9 months and seemed perfectly cured.

Discussion

The presence of mucopolysaccharides was shown by Alcian blue, toluidine blue and P A S staining methods. It was also shown that hyaluronidase dissolves acid mucopolysaccharides, hyaluronic acid and chondroitin sulphate. So the chemical structure of the lesions were demonstrated. It was also seen that fibrin takes part in the formation of the membranes. Owing to its richness in acid mucopolysaccharides, the umbilical cord was used as control material. Although in some reactions there were slight differences, probably due to technical



Fig 5

Acid mucopolysaccharides are entirely dissolved by hyaluronidase digestion while P.A.S. material is not dissolved (arrows) (Alcian blue + P.A.S. $\times 75$)



Fig 6

Wavy appearance of fine fibrine bands in the ligamentous membranes (arrows) (Phospho tungstic acid + hematoxylin $\times 75$)

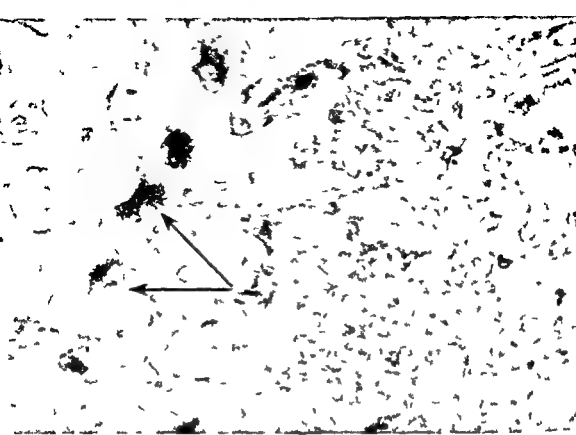


Fig 4

Section after hyaluronidase digestion The right part of the slide is pale due to digestion proving the presence of acid mucopolysaccharides while the non treated part remains darker (arrows) (Alcian blue $\times 400$)

over a period of three and half months The patient was seen after 8 months and seemed perfectly cured

Discussion

The presence of mucopolysaccharides was shown by Alcian blue toluidine blue and P A S staining methods It was also shown that hyaluronidase dissolves acid mucopolysaccharides hyaluronic acid and chondroitin sulphate So the chemical structure of the lesions were demonstrated It was also seen that fibrin takes part in the formation of the membranes Owing to its richness in acid mucopolysaccharides the umbilical cord was used as control material Although in some reactions there were slight differences probably due to technical



Fig 5

Acid mucopolysaccharides are entirely dissolved by hyaluronidase digestion while I A S material is not dissolved (arrows) (Alcian blue + P A S $\times 25$)

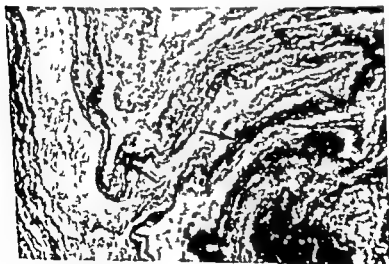


Fig 6

Wavy appearance of fine fibrine bands in the ligneous membranes (arrows) (Ph phosphotungstic acid + hematoxylin, $\times 25$)

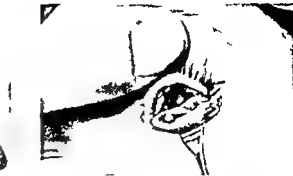


Fig 7

Case I Right eye Thick ligneous membranes covering the tarsal conjunctiva of both lids

Fig 8

Case I Left eye Membrane formation and bleeding after attempt of removal of the membrane

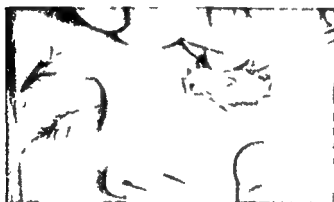


Fig 9

Case II Thick ligneous membranes on both tarsal conjunctivas

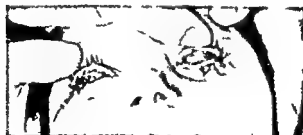


Fig 10

Case II: Bleeding of the tarsal conjunctivae after removal of the membranes



Fig 11

Case II Both upper tarsal conjunctivae looking perfectly normal after treatment



Fig 12

Case II Normal appearance of both lower tarsal conjunctivae after treatment



Fig 13

Case II Eight months after the treatment The condition is completely cured no membranes kerato iridocyclitis healed leaving a simple scar covering 1/3 of the right lower cornea



Fig 7

Case I Right eye Thick ligneous membranes covering the tarsal conjunctiva of both lids



Fig 8

Case I Left eye Membrane formation and bleeding after attempt of removal of the membrane

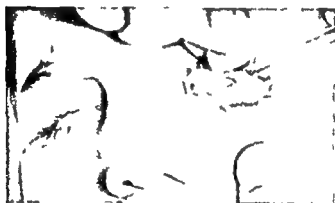


Fig 9

Case II Thick ligneous membranes on both tarsal conjunctivas



Fig 10

Case II Bleeding of the tarsal conjunctivae after removal of the membranes



Fig 11

Case II Both upper tarsal conjunctivae looking perfectly normal after treatment



Fig 12

Case II Normal appearance of both lower tarsal conjunctivae after treatment



Fig 13

Case II Eight months after the treatment The condition is completely cured no membranes kerato iridocyclitis healed leaving a simple scar covering 1/3 of the right lower cornea

details the special staining methods gave satisfactory results throwing light on the histochemical constitution of ligneous conjunctivitis

The treatment with hyaluronidase and alpha chymotrypsine was successful and gave identical results as those obtained by François. His method of treatment based on histochemical findings seems to be most effective in this rare disease the etiology and treatment of which were hitherto unknown

Summary

Histochemical and histopathological examinations were carried out on two cases of ligneous conjunctivitis observed at the Department of Ophthalmology Hacettepe University Faculty of Medicine Ankara Turkey. Special staining methods demonstrated the presence of acid mucopolysaccharides confirming and emphasizing the results which François and his co workers described for the first time in their recent publications

The second case was successfully treated by local applications of hyaluronidase combined with alpha chymotrypsine also as advocated by François for this disease in which all previous treatments have been unsuccessful

Acknowledgement

We are indebted to Gorenç Ciliz M.D. (Department of Biochemistry Hacettepe University) who applied the Anthrone Method for the dosage of mucopolysaccharides in the urine

References

- Duke Elder S. System of Ophthalmology. Ed Kimpton London Vol 5 Pt 1 p 95 1965
- François J. Noyer A. Hanssens M. & Victoria Troncoso V. Nouvelle observation histo chimique de la conjonctivite ligneuse. Ann d'Oculistique 199 952 1966
- François J. Hanssens M. & Victoria Troncoso V. Conjonctivite ligneuse à fausse membrane. Etude clinique histo pathologique et thérapeutique. Ann d'Oculistique 200 1066 1966
- François J. Hanssens M. & Victoria Troncoso V. La conjonctivite ligneuse. Ophthalmologica 154 410 1967
- François J. Victoria Troncoso V. Treatment of ligneous conjunctivitis. Amer J Ophthalmol 63 674 1965

- Gridley W F Manual of Histologic and Special Staining Techniques 2nd Edition, Blakiston Div New York, 1960
- Hery J Demailly Ph & Dhermy P Conjunctivite ligueuse Bull Soc Ophtal France 66 977 1966
- Katsourakis N & Roussas J Ligneous conjunctivitis Bull Soc. Hellen Ophtal 54 93 1966
- Mc Manus J F & Mowry R W - Staining Methods Histologic and Histochemical Hoeber New York 1960
- Marcione G A & Lijo-Pavia J J The Lijo Pavia syndrome (woody conjunctivitis) Treatment and nomenclature Rev Oto-Neuro Ofal (Buenos Aires) 41 53 1966
- Pearse A G E Histochemistry Theoretical and Applied 2nd Ed Little Brown Co., Boston 1960
- Spaeth G L Chronic membranous conjunctivitis Amer J Ophthal 64 300 1967

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A FAMILY WITH BILATERAL SYMMETRICAL SECTORAL PIGMENTARY RETINAL LESION

BY

H FLEDELIUS & S E SIMONSEN

Bilateral symmetrical sectoral pigmentary lesion of the retina was first described by Bietti (8) in 1937. Since then new reports have not been numerous. Thus Haase & Hellner (13) were able to collect from literature only 23 cases of sectoral pigmentary retinopathies and in some of these the fundi showed unilateral pigmentation or otherwise nonsymmetrical occurrence. In Scandinavia the subject has not been treated in detail before.

This report deals with three patients, members of the same family, with symmetrical sectoral pigmentary retinal lesion. Since the prognosis of the disease is not well established by follow up studies of single cases, we have found it of interest to repeat examinations six years after the initial ones.

Case no 1

A woman aged 59 years with hemeralopic complaints for more than 25 years. There were no hereditary disorders in the family and her parents were not consanguineous. Since the age of fifty she suffered from some headache and dizziness due to a benign hypertension, she was therefore admitted to an ophthalmologist who discovered her retinal disorder. The further investigation was performed in the Eye Clinic of Rigshospitalet.

1962 Visual acuity < 6/6 in both eyes with correction. Colour vision normal (Ishihara diagrams), slit lamp examination and intraocular tension normal.

Perimetry with Goldmann showed visual field defects in the upper halves (fig 7) corresponding to the affected lower retinal quadrants.

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Fig 1

Fundi of patient no 1 (right eye above left eye below)

Fundi showed almost identical pictures with normal discs and macular areas and normal vessels upwards but vascular attenuation in the two lower quadrants corresponding to a demarcated semilunar yellowish area - extending from just below the discs towards the periphery - with scattered pigmentation partly of bone corpuscle type

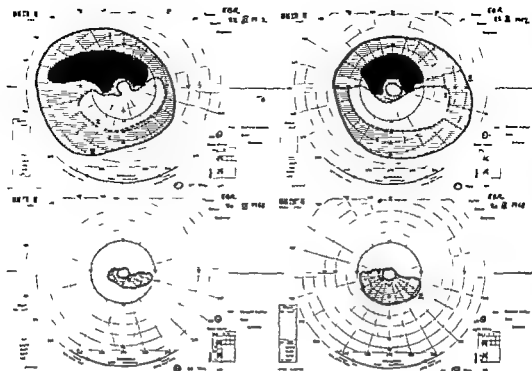


Fig 2

Visual fields of patient no 1 showing restriction from 1962 (above) to 1968 (below)

ERG a m Harpe Subnormal b waves in both eyes

X ray of cranium and sella turcica normal

WR negative

Audiometry Loss of perception for high and for low hz

Vestibular function and neurological examination normal

1968 Visual acuity 6/9 in both eyes with corr Colour vision (Ishihara) slit lamp examination and intraocular tension still normal Ophthalmoscopy showed optic discs more pale than in 1962 and some increase of the demarcated pigmented retinal areas in the lower quadrants (fig 1) Visual fields showed further restriction (fig 2)

ERG Subnormal b waves (amplitude 100 μ V)

Adaptometry a m Goldmann Wecker Monophasic curve with loss of the scotopic part

Case no 2

A 38 year old healthy man without eye complaints especially no hemeralopic He is the son of patient no 1

1962 Visual acuity 6/6 in both eyes Colour vision normal (Ishihara diagrams) slit lamp examination and intraocular tension normal

His fundi showed normal discs normal macular areas and normal upper retinal quadrants but in the lower quadrants a semilunar yellowish area was seen with thin vessels and irregular pigmentations mostly pronounced in the right eye

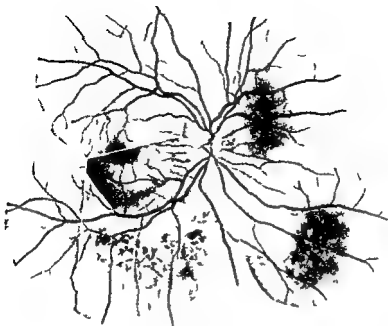


Fig 3
Fundi of patient no 2 (right eye above left eye below)

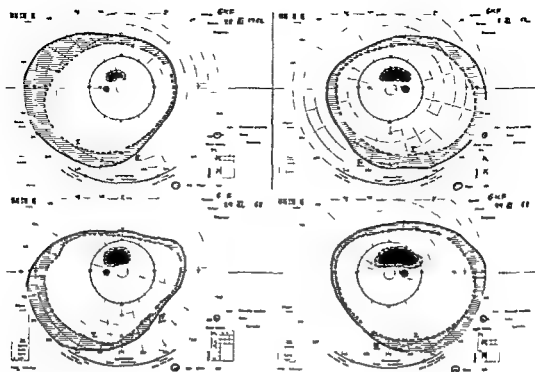


Fig 4

Visual fields of patient no 2 in 1962 (above) and 1963 (below)

Perimetry a m Goldmann showed small islet scotomas 15-20° above the point of fixation (fig 4) corresponding to the retinal lesions

ERG a m Karpe Normal b waves (amplitude 210 μ V)

WR negative

1964 Still no eye complaints

Examinations showed results as in 1962 except increase of the affected areas and visual field defects (fig 3-4) ERG was subnormal (b wave 160 μ V) in the right eye and normal (b wave 250 μ V) in the less affected left eye

Adaptometry a m Goldmann-Wecker normal

Case no 3

A 61 year old man the only brother of case no 1 Apart from slight hemeralopic complaints he had no eye trouble His retinopathy was discovered in 1964

Visual acuity 6/6 in both eyes with corr

Colour vision normal (Ishihara diagrams) Slit lamp examination showed incipient cortical cataract Intraocular tension normal

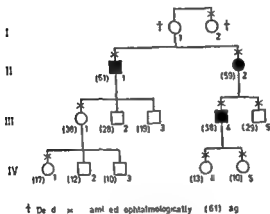
Ophthalmoscopy showed normal optic discs and macular areas In the lower retinal quadrants in both eyes well demarcated yellowish areas with pigmentation very much like the fundi of case no 1

The visual field defects are shown in fig 5

ERG a m Karpe showed minimal responses (b waves 30 μ V)



Fig 5
Visual fields of patient no 3 in 1968



† Died * died ophthalmologically (61) age

Fig 6
The family scheme Cases 1 2 and 3 are indicated with black (II 2 III 4 and II 1)
Bilateral sectoral pigmentary retinopathy could not be demonstrated in the rest
of the family

Discussion

Franceschetti François & Babel (9) (1963) classify the *Retinopathie pigmentaire en secteur* among the peripheral tapetoretinal degenerations. This corresponds to Duke Elder's (1) classification of sectoral pigmentary dystrophy as a peripheral dystrophy part of the subgroup atypical pigmentary lesions.

About thirty cases of bilateral symmetrical pigmentary retinopathy have been reported since Bietti's (3) original statement. Several authors suggest that the disease is much more common than indicated by the number of known cases.

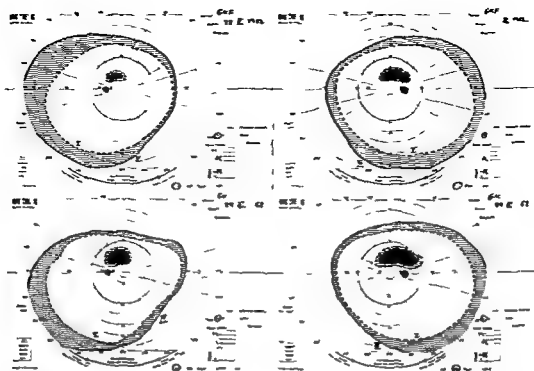


Fig 4

Visual fields of patient no 2 in 1962 (above) and 1968 (below)

Perimetry a. m. Goldmann showed small islet scotomas 15-20 above the point of fixation (fig 4) corresponding to the retinal lesions

ERG a. m. Karpe Normal b-waves (amplitude 270 μV)

WR negative

1968 Still no eye complaints

Examinations showed results as in 1962 except increase of the affected areas and visual field defects (fig 3-4) ERG was subnormal (b-wave 160 μV) in the right eye and normal (b-wave 250 μV) in the less affected left eye

Adaptome cv a. m. Goldmann-Wecker normal

Case no 3

A 61 year-old man, the only brother of case no 1. Apart from slight hemeralopic complaints he had no eye trouble. His retinopathy was discovered in 1968

Visual acuity 6/6 in both eyes with corr

Colour vision normal (Ishihara diagrams) Slit lamp examination showed incipient cortical cataract. Intraocular tension normal.

Ophthalmoscopy showed normal optic discs and macular areas. In the lower retinal quadrants in both eyes well demarcated yellowish areas with pigmentation, very much like the fundi of case no 1

The visual field defects are shown in fig 5

ERG a. m. Karpe showed minimal responses (b-waves 30 μV)

It is well known that defects in cochlear and vestibular function appear frequently in patients with typical retinitis pigmentosa. Thus Bruno & Iolo Spada (5) examining 30 patients with typical retinitis pigmentosa found a high incidence of audiometric and also olfactory changes suggesting a causal relationship between three neuro epithelial disorders. Some cases of bilateral symmetrical pigmentary lesion show defects of the auditory function too e.g. surdomutitas (3-24) and surditas (14). Our cases no. 1 and 2 were examined otologically but no specific defects were discovered.

The patients with sectoral pigmentary retinopathies are in general otherwise healthy and the disease does not regularly take part in syndromes. A few exceptions do however exist. Morgagni Stewart Morel syndrome in Rubino's (23) patient and Lawrence Moon Biedl syndrome in Tavolara's (26) case.

The etiological problems are briefly discussed by Kuper (14) who mentions the various hypotheses. The abiotrophic concept is that usually advanced. A primary hereditary vascular degeneration affecting only a part of the retina has also been proposed. Our fundus pictures (figs 1 and 3) seem to show some relation of the pigmentary disturbances to the retinal vascular tree. It has also been emphasized that the retinal area usually affected first corresponds to the region of the fetal cleft in the eyeball but other initial retinal locations of the disorder have been reported.

Summary

Three cases of hereditary bilateral symmetrical retinal pigmentary lesion are reported. The disease is rare - about 30 cases are known. Two of our cases have been re-examined after an interval of six years both showing some progression. The few symptoms and the good prognosis is however emphasized especially when compared with the typical retinitis pigmentosa.

Acknowledgments

We wish to thank Dr V. Ohrt for the examination of patient III 5 in the family scheme and Dr V. Dreyer for the adaptometries made.

References

1. Agostoni I. Acta Ophthalm. 1968 46: 41-48.
2. Batra M. V. Brit. J. Ophthalm. 1966 50: 734-735.

because the symptoms are too mild to make the patient consult an ophthalmologist. Most cases are discovered – like ours – by accidental examination.

The characteristics of the sectoral pigmentary retinal lesions can be briefly summarized. The disease is usually limited to the lower retinal quadrants – preferentially the inferonasal ones – and is usually of bilateral symmetrical appearance. It is said to be non progressive or very slowly progressive with only slight disturbance of dark adaptation and with good visual acuity. The visual field defects usually correspond with the retinal lesions. The retinal vessels are narrow only in the affected areas.

ERG can be recorded: the b waves show normal or subnormal values in younger and middle-aged patients while they are markedly reduced in the elderly. The dark adaptation curves are likewise normal in younger patients but tend to be monophasic and hemeralopic with increasing age. For further details concerning ERG and adaptometry in this disease we can point out the references (6, 8, 10, 13, 14, 15, 17, 24, 28). The disease is hereditary, primarily with autosomal dominant transmission (12, 13, 14, 17, 18, 19) but recessive inheritance (3, 24) and sex-linked transmission (9) have been reported. Our family scheme (fig. 6) corresponds with the dominant transmission.

In comparison with the typical retinitis pigmentosa the differences are striking. In the latter there is pigmentary disturbance in the whole periphery with early clinical progression leading to impaired vision. ERG is abolished, the adaptation curve is flattened, and colour vision will be affected.

In contrast to this the prognosis of the bilateral symmetrical sectoral pigmentary retinopathy is regarded as quite good – as mentioned above. This is based on the observation of the extent of retinal involvement in the different age groups in families with the disorder (13, 17, 18, 19). Thus Haase & Hellner report on three children younger than ten years with only slight pigmentary disturbances; their elder sisters and brothers showed increasing involvement and the retinal lesions were pronounced in the eldest members of the family. In a 73-year-old woman in the family reported by Lisch (18) only tubular visual fields and a peripheral zone downwards were preserved.

It is however important also to estimate the prognosis of the disease by re-examinations of already known cases. Klier's (16) 44-year-old patient showed progression of the visual field defect by perimetry repeated after 10 weeks while Graham's (11) 28-year-old patient remained absolutely unchanged during nine months. Our case no. 1 showed pronounced deterioration during six years subjectively as well as by ophthalmoscopy, ERG and perimetry (fig. 2) while case no. 2 showed only slight progression in the same period (fig. 4). The small number of observations here and in other reports do not allow exact prognostic conclusions, but it still seems justified to emphasize the benign clinical course with slow progression – especially as compared with the prognosis of the typical retinitis pigmentosa.

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DYNAMIC TONOMETRY

II Methods of corneal indentation pulse registration

BY

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The pulsesynchronous changes in eye tension may be studied in detail by use of the dynamic tonometer which is an improved Schiotz electronic tonometer (Horven 1968). In its present state this instrument yields an output of one mV per μ plunger deflection as shown in Fig 1. As suggested by Bron *et al* (1967) the recorded pulsations in eye tension may be regarded as an indentation pulse. The difference between the highest and lowest points on each wave gives the amplitude of the indentation pulse which is recorded in mV and converted into microns of plunger deflection. As known the Schiotz weight tonometer yields a plunger deflection of 50 μ between each scale reading.

The purpose of the present paper is to study in which manner the various tonometry parameters V , P , P_t and ΔV may be applied to the microns of indentation pulse amplitudes at various eye tension levels.

V_c

Friedenwald (1957) presented in his table IV the volume of corneal indentation (V_c) in mm^3 at half a scale reading (R) intervals. This offers the opportunity to calculate the volume of corneal indentation which corresponds to one μ plun

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- 3 *Bietti G* Boll Oculist 1937 16 1159-1244
- 4 *Biro I* Amer J Ophthal 1963 55 1176-1179
- 5 *Bruno G* & *Iolo Spada G* Boll Oculist 1962 41 611-625
- 6 *Dieterle P* Arch Ophthal 1954 14 707-716
- 7 *Duke Elder* System of Ophthalmology Vol 1 London 1967 574-596
- 8 *Franceschetti A* Ophthalmologica 1965 149 266-276
- 9 *Franceschetti A* *François J* & *Babel J* Les Heredo degenerescences Choriorétiennes Masson et C^{ie} Paris 1963 325-338
- 10 *Goodman G* & *Gunkel R D* Amer J Ophthal 1958 46 142-178
- 11 *Graham M V* Brit J Ophthal 1963 47 682-686
- 12 *Grut ner P* J Genet Hum 1963 12 71-82
- 13 *Haase W* & *Hellner K A* Klin Mbl Augenhk 1965 147 365-375
- 14 *Hommer K* v *Graef* Arch Ophthal 1959 161 16-26
- 15 *Karpe G* The basis of clinical Electrorétinography Acta Ophthal 1945 suppl XXIV
- 16 *Klier A* Klin Mbl Augenhk 1965 147 361 365
- 17 *Kuper J* Klin Mbl Augenhk 1960 156 91-102
- 18 *Lisch K* Forschung und Praxis 1955 10 54-58
- 19 *Lisch K* Med Mschr 1960 14 720-725
- 20 *Manfredini U* & *Manuelli G F* Ann Ottal 1966 42 669 678
- 21 *Mighor M* *Redi F* *Spinelli D* *De Molfetta V* & *Polenghi F* Ophthalmologica 1967 154 411-422
- 22 *Ragnetti E* From Excerpta Med Ophthal 1963 470
- 23 *Rubino A* Giorn Ital Oftal 1949 2 411-426
- 24 *Straub W* Klin Mbl Augenhk 1961 Beiheft 36
- 25 *Streif E B* & *Hermann C* Bull Soc Franc Ophthal 1950 63 300-305
- 26 *Tatolara L* Giorn Ital Oftal 1949 2 52-58
- 27 *Verrey F* Ophthalmologica 1947 114 278-280
- 28 *Vukovich V* v *Graef* Arch Ophthal 1959 161 27-31

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DYNAMIC TONOMETRY

II Methods of corneal indentation pulse registration

BY

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The pulsesynchronous changes in eye tension may be studied in detail by use of the dynamic tonometer which is an improved Schiøtz electronic tonometer (Hørvén 1968). In its present state this instrument yields an output of one mV per μ plunger deflection as shown in Fig. 1. As suggested by Bron *et al.* (1967) the recorded pulsations in eye tension may be regarded as an indentation pulse. The difference between the highest and lowest points on each wave gives the amplitude of the indentation pulse which is recorded in mV and converted into microns of plunger deflection. As known the Schiøtz weight tonometer yields a plunger deflection of 50 μ between each scale reading.

The purpose of the present paper is to study in which manner the various tonometry parameters V , P , P_1 and ΔV may be applied to the microns of indentation pulse amplitudes at various eye tension levels.

V_0

Friedenwald (1951) presented in his table IV the volume of corneal indentation (V) in mm^3 at half a scale reading (R) intervals. This offers the opportunity to calculate the volume of corneal indentation which corresponds to one μ plun

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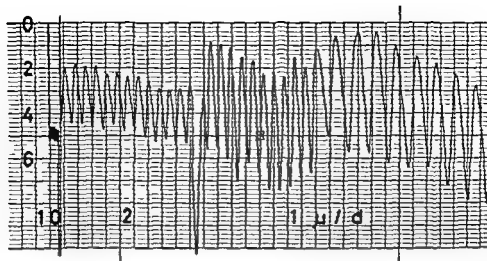


Fig 1

Normal indentation pulse of 2 μ amplitude recorded at eye tension $R = 5$ with the sensitivity settings 10 2 and 1 mV per paper division. One mV equals 1 μ plunger deflection. Paper speed 1 5 and 10 mm per second.

ger deflection (ΔV_c) at different eye tension levels. The calculation of ΔV_c is performed in the following manner at $R = 0$ and $R = 13$ measured with the 5.5 g plunger weight.

$$\Delta V_{c(0)} = \frac{V_{c(0.5)} - V_{c(0)}}{25} = \frac{4.96 - 4.38}{25} = 0.0232 \text{ mm}^3/\mu$$

$$\Delta V_{c(13)} = \frac{V_{c(13.5)} - V_{c(13)}}{25} = \frac{33.43 - 31.87}{25} = 0.0624 \text{ mm}^3/\mu$$

The calculated ΔV_c values at $R = 0$ and $R = 13$ are actually the mean ΔV_c values of $R = 0-0.5$ and $R = 13-13.5$. No correction of this fact seems however necessary. When performing dynamic tonometry the eye tension is first recorded followed by indentation pulse amplitude registrations. As known the intraocular pressure demonstrates a moderate decrease during the period the tonometer is resting on the eye. Accordingly the indentation pulse is actually recorded at eye tension $R = 0.05$ and $R = 13.135$. The above easy way of ΔV_c calculation seems therefore appropriate for practical use. As demonstrated ΔV_c in mm^3/μ increases with increasing values of R . An excellent linear relationship is demonstrated between the ΔV_c values in mm^3/μ plotted versus R as shown in Fig 2. The relationship between ΔV_c and R may therefore be expressed through the equation $\Delta V_c = a + b \cdot R$. The numerical values of a and b have been calculated for the various plunger weights and the

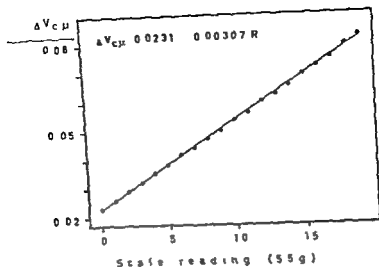


Fig 2

Corneal indentation volume (ΔV_c) in mm^3 per μ plunger deflection plotted versus scale readings

actual correlation between the calculated ΔV_c values and the straight line is given by the correlation coefficient r

$$(1) \Delta V = 0.00231 + 0.00307 R \quad (50 \text{ g } r = 0.9996)$$

$$(2) \Delta V = 0.0188 + 0.00336 R \quad (75 \text{ g } r = 0.9994)$$

$$(3) \Delta V = 0.0149 + 0.00345 R \quad (10 \text{ g } r = 0.9987)$$

Example The change in corneal indentation volume (ΔV_c) which corresponds to an indentation pulse of 30μ amplitude recorded at $R = 5$ with the 55 g plunger weight is calculated as follows

$$\Delta V = 30 \Delta V_c = 30(0.00231 + 0.00307 \cdot 5) = 1.15 \text{ mm}^3$$

The V values of Friedenwald were calculated by use of the equation

$$(4) \log P_t = B - \frac{1}{0.016} \log V_c$$

In order to obtain an estimate of B the V value at $R = 5$ was calculated by use of the formula $\log P = \log P_t - k \cdot V_c$. A P value of 17.3 mm Hg and the average normal ocular rigidity coefficient value of 0.0215 were used these values had previously been determined by Friedenwald. The factor B could then be estimated by insertion of this calculated V value in equation (4). Friedenwald's procedure of V calculation by equation (4) depends therefore not

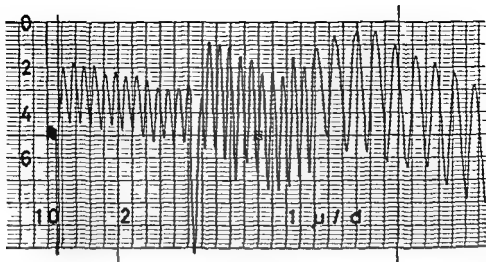


Fig 1

Normal indentation pulse of 2 μ amplitude recorded at eye tension $R = 5$ with the sensitivity settings 10 2 and 1 mV per paper division One mV equals 1 μ plunger deflection Paper speed 1 5 and 10 mm per second

ger deflection (ΔV_c) at different eye tension levels The calculation of ΔV_c is performed in the following manner at $R = 0$ and $R = 13$ measured with the 5.5 g plunger weight

$$\Delta V_{c(0)} = \frac{V_{c(0.5)} - V_{c(0)}}{25} = \frac{4.96 - 4.35}{25} = 0.0232 \text{ mm}^3/\mu$$

$$\Delta V_{c(13)} = \frac{V_{c(13.5)} - V_{c(13)}}{25} = \frac{33.43 - 31.97}{25} = 0.0624 \text{ mm}^3/\mu$$

The calculated ΔV_c values at $R = 0$ and $R = 13$ are actually the mean ΔV_c values of $R = 0-0.5$ and $R = 13-13.5$. No correction of this fact seems however necessary. When performing dynamic tonometry the eye tension is first recorded followed by indentation pulse amplitude registrations. As known the intraocular pressure demonstrates a moderate decrease during the period the tonometer is resting on the eye. Accordingly the indentation pulse is actually recorded at eye tension $R = 0.05$ and $R = 13.135$. The above easy way of ΔV_c calculation seems therefore appropriate for practical use. As demonstrated $\Delta V_{c\mu}$ in mm^3/μ increases with increasing values of R . An excellent linear relationship is demonstrated between the ΔV_c values in mm^3/μ plotted versus R as shown in Fig 2. The relationship between ΔV_c and R may therefore be expressed through the equation $\Delta V_c = a + b \cdot R$. The numerical values of a and b have been calculated for the various plunger weights and the

As demonstrated in Fig 3 (top) the ΔP_o values increase markedly with increasing intraocular pressure i.e. with decrease in R. An excellent linear correlation is demonstrated (Fig 3 bottom) when the various $\log \Delta P_o$ values are plotted versus R fitting the equation $\log \Delta P_o = a + b R^{-2}$. The values of a and b have been calculated for the various plunger weights as follows

$$(8) \log \Delta P_o = 1.1328 - 0.0138 R^{-2} \quad (5.5 \text{ g } r = 0.9995)$$

$$(9) \log \Delta P_o = 1.2671 - 0.0694 R^{-2} \quad (7.5 \text{ g } r = 0.9995)$$

$$(10) \log \Delta P_o = 1.3874 - 0.0660 R^{-2} \quad (10 \text{ g } r = 0.9995)$$

Example The ΔP_o value which corresponds to an indentation pulse of 30μ amplitude recorded at $R = 5$ with the 5.5 g plunger weight is calculated as follows

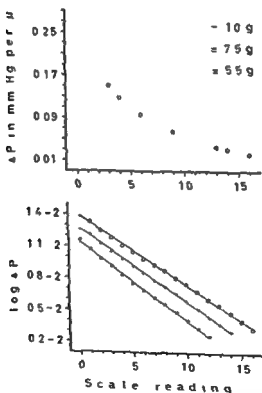


Fig 3

Changes in intraocular pressure (ΔP) in mm Hg per μ plunger deflection at various scale readings (top) $\log \Delta P_o$ plotted versus scale readings demonstration of excellent linear correlation at all plunger weights (bottom)

only on the validity of his P_t values but also on the rigidity coefficient value of 0.0215. As demonstrated by Ytteborg (1960), Eisenlohr et al (1962) Hetland Eriksen (1966) and others Friedenwald's rigidity coefficient value of 0.0215 is probably too large.

By use of an experimental set up on freshly enucleated human eyes Hetland Eriksen measured the volume of displaced fluid which occurred by mechanical Schiotz tonometry (V_t) and found higher values than reported by Friedenwald. Hetland Eriksen's data permits calculation of the volume of displaced fluid in mm^3 which corresponds to one μ plunger deflection ($\Delta V_{t\mu}$) at various eye tension levels. A fair linear relationship is demonstrated when the $\Delta V_{t\mu}$ values are plotted versus R which offers the opportunity of presenting the Hetland Eriksen data by the following equations:

$$(5) \Delta V_{t\mu} = 0.0269 + 0.00317 R \quad (5.5 \text{ g } r = 0.9846)$$

$$(6) \Delta V_t = 0.0247 + 0.00271 R \quad (7.5 \text{ g } r = 0.9851)$$

$$(7) \Delta V_{t\mu} = 0.0208 + 0.00282 R \quad (10 \text{ g } r = 0.9950)$$

Example: The volume of displaced fluid (ΔV_t) which corresponds to an indentation pulse of 30 μ amplitude recorded at $R = 5$ with the 5.5 g plunger weight will be

$$\Delta V_t \approx 30 \Delta V_{t\mu} = 30(0.0269 + 0.00317 \cdot 5) = 1.28 \text{ mm}^3$$

Accordingly the results obtained by use of Hetland Eriksen's data yield roughly 10% larger values than the results obtained by use of Friedenwald's data.

P_o

Friedenwald calculated the intraocular pressure before tonometry (P_o) by use of the formula $\log P_o = \log P_t - k/V_e$ where k is the ocular rigidity coefficient of 0.0215. As mentioned above Friedenwald's V_e values are probably too small and his rigidity coefficient value of 0.0215 probably too large. These discrepancies will however to some extent work against each other in the product k/V_e . His P_o values are therefore accepted for practical use without further reservations.

The change in intraocular pressure before tonometry which corresponds to a plunger deflection of one μ (ΔP_o) is calculated at $R = 2$ with the 5.5 g plunger weight as follows:

$$\Delta P_{o(\mu)} = \frac{P_{o(2)} - P_{o(1)}}{25} = \frac{28.97 - 26.56}{25} \approx 0.0964 \text{ mm Hg}/\mu$$

In this manner the various ΔP_o values may be calculated at all tension levels.

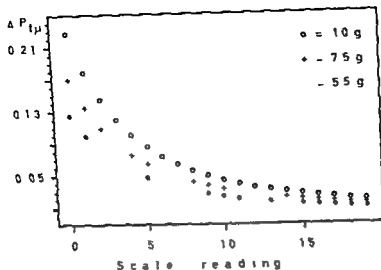


Fig 4

Changes in intraocular pressure (ΔP_t) in mm Hg per μ plunger deflection at various scale readings

pressure as shown in Fig 4. A linear relationship was not demonstrated neither between ΔP_t plotted versus R nor between $\log \Delta P_t$ plotted versus R . The ΔP_t values are therefore given in mm Hg per μ plunger deflection at the various eye tension levels and with the three plunger weights in Table II.

ΔV

Friedenwald calculated the change in ocular volume (ΔV) for various plunger weights when the tonometer reading falls from 0 to R by use of the equation

$$(11) \quad \Delta V = \frac{1}{k} \log \frac{P_t}{P_{IR}} + V_R - V$$

A fair linear relationship is demonstrated when plotting the ΔV values versus R as shown in Fig 5. The ΔV points are not however distributed at random around this straight line but yields a definite upward concave slope suggesting that the data would better fit into the equation $y = a + bx + cx^2$. In Fig 6 this equation has been used with $x = 0$ at $R = 8.0$. An excellent correlation is noted. For a practical purpose therefore ΔV may be calculated directly from R with a fair degree of accuracy by use of this equation with the following values for a , b and c for various plunger weights.

$$\log \Delta P_i = 1.1328 - 0.0738 \cdot 5 - 2 = 0.7638 - 2$$

$$\Delta P_{0i} = 0.058 \text{ mm Hg}/\mu$$

$$\Delta P_0 = 30 \quad \Delta P_0 = 30 \cdot 0.058 = 1.74 \text{ mm Hg}$$

Table I offers the ΔP_0 values in mm Hg per μ plunger deflection which may be calculated by use of equations (8) (9) (10) for various scale readings and plunger weights

P_i

The change in intraocular pressure during tonometry which corresponds to a plunger deflection of one μ (ΔP_i) may be calculated by use of Friedenwald's P_i data at the various eye tension levels in an identical manner as for ΔP_0 . The $\Delta P_{i\mu}$ values demonstrate a marked increase with increasing intraocular

Table I
 ΔP_i in mm Hg per μ plunger deflection

R	5.5 g	7.5 g	10 g	R	5.5 g	7.5 g	10 g
0	0.1359	0.1850	0.2440	10	0.0248	0.0374	0.0534
0.5	0.1258	0.1709	0.2261	10.5	0.0228	0.0345	0.0495
1	0.1146	0.1577	0.2096	11	0.0209	0.0319	0.0459
1.5	0.1052	0.1455	0.1943	11.5	0.0192	0.0294	0.0425
2	0.0967	0.1344	0.1801	12	0.0177	0.0272	0.0394
2.5	0.0889	0.1241	0.1669	12.5	0.0162	0.0251	0.0365
3	0.0816	0.1145	0.1546	13	0.0149	0.0232	0.0338
3.5	0.0749	0.1057	0.1433	13.5	0.0137	0.0214	0.0314
4	0.0688	0.0976	0.1328	14	0.0126	0.0197	0.0291
4.5	0.0632	0.0901	0.1231	14.5	0.0116	0.0182	0.0270
5	0.0580	0.0832	0.1141	15	0.0106	0.0169	0.0250
5.5	0.0533	0.0768	0.1059	15.5	0.0097	0.0155	0.0231
6	0.0490	0.0708	0.0980	16	0.0090	0.0143	0.0215
6.5	0.0450	0.0655	0.0908	16.5	0.0082	0.0132	0.0199
7	0.0413	0.0604	0.0842	17	0.0076	0.0122	0.0184
7.5	0.0380	0.0559	0.0780	17.5	0.0069	0.0113	0.0171
8	0.0349	0.0511	0.0724	18	0.0064	0.0104	0.0158
8.5	0.0320	0.0476	0.0671	18.5	0.0059	0.0096	0.0147
9	0.0294	0.0439	0.0622	19	0.0054	0.0089	0.0136
9.5	0.0270	0.0405	0.0576	19.5	0.0049	0.0082	0.0126

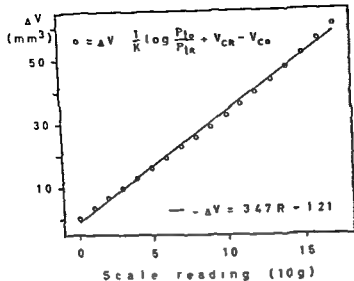


Fig 5

Changes in ocular volume (ΔV) in mm³ when the plunger moves from 0 to R plotted versus scale readings a fair linear correlationship is noted

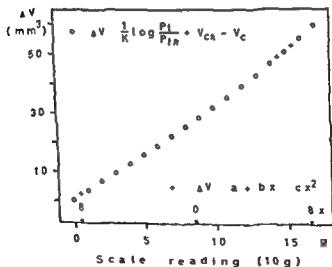


Fig 6

Changes in ocular volume (ΔV) in mm when the plunger moves from 0 to R as given by Friedenwald (a) Theoretically calculated ΔV values fitting the equation $y = a + b x + c x^2$ (+)

Table II
 ΔP_{μ} in mm Hg per μ plunger deflection

R	5.5 g	7.5 g	10 g	R	5.5 g	7.5 g	10 g
0	0.1244	0.1696	0.2264	10	0.0248	0.0336	0.0448
0.5	0.1104	0.1504	0.2008	10.5	0.0232	0.0316	0.0424
1	0.0984	0.1344	0.1888	11	0.0220	0.0300	0.0400
1.5	0.0884	0.1204	0.1608	11.5	0.0208	0.0288	0.0384
2	0.0796	0.1088	0.1448	12	0.0200	0.0272	0.0360
2.5	0.0724	0.0984	0.1312	12.5	0.0192	0.0256	0.0344
3	0.0656	0.0900	0.1200	13	0.0180	0.0248	0.0332
3.5	0.0604	0.0820	0.1096	13.5	0.0172	0.0236	0.0312
4	0.0552	0.0756	0.1004	14	0.0164	0.0224	0.0300
4.5	0.0512	0.0696	0.0928	14.5	0.0156	0.0212	0.0284
5	0.0472	0.0640	0.0860	15	0.0152	0.0208	0.0276
5.5	0.0436	0.0596	0.0792	15.5	0.0144	0.0196	0.0260
6	0.0408	0.0556	0.0740	16	0.0140	0.0188	0.0252
6.5	0.0380	0.0516	0.0688	16.5	0.0132	0.0180	0.0244
7	0.0352	0.0484	0.0644	17	0.0128	0.0176	0.0236
7.5	0.0332	0.0452	0.0604	17.5	0.0120	0.0168	0.0220
8	0.0312	0.0424	0.0568	18	0.0120	0.0160	0.0216
8.5	0.0292	0.0400	0.0532	18.5	0.0112	0.0156	0.0204
9	0.0276	0.0376	0.0500	19	0.0112	0.0148	0.0200
9.5	0.0260	0.0356	0.0472	19.5	0.0104	0.0144	0.0192

$$(12) \Delta V = 22.8758 + 3.5945 x + 0.0204 x^2 \quad (5.5 \text{ g } x = R - 6.5)$$

$$(13) \Delta V = 25.1675 + 3.5370 x + 0.0344 x^2 \quad (7.5 \text{ g } x = R - 7.5)$$

$$(14) \Delta V = 27.2198 + 3.4587 x + 0.0409 x^2 \quad (10 \text{ g } x = R - 8.5)$$

Example ΔV at $R = 5$ respective $R = 10$ with the 5.5 g plunger weight is calculated as follows

$$x = R - 6.5 = 5 - 6.5 = -1.5$$

$$\Delta V = 22.8758 + 3.5945 (-1.5) + 0.0204 (-1.5)^2 = 17.53 \text{ mm}^3$$

$$x = R - 6.5 = 10 - 6.5 = 3.5$$

$$\Delta V = 22.8758 + 3.5945 (3.5) + 0.0204 (3.5)^2 = 35.71 \text{ mm}^3$$

It is stressed that even if the correlation between the equation $y = a + bx + cx^2$ and Friedenwald's ΔV data is excellent the two curves are not identical and a minor discrepancy between their various decimal values should be expected. In the following therefore Friedenwald's original data as listed in his Table VII are used for calculation of ΔV_{μ} i.e. the change in ocular volume which yields a plunger deflection of one μ at various eye tension levels. The

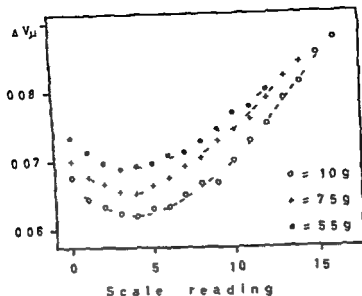


Fig 7

Change in ocular volume in mm^3 per μ plunger deflection (ΔV_{μ}) calculated from Friedenwald's data at various scale readings

If $R = 0.5 + R_1$ equation (15) may be used to calculate the various ΔV differences at all tension levels. Dividing the results by 25 gives the various ΔV_{μ} values in mm^3 per μ plunger deflection.

As suggested by Friedenwald the pressure volume relationship of the eye may be expressed by the equation

$$k \Delta V = \log P - \log P_1 \text{ which gives } \Delta V = \frac{1}{k} \log \frac{P}{P_1}$$

In equation (15) the first part of the formula

$\left(\frac{1}{k} \log \frac{P_R}{P_{1R}} \right)$ will therefore indicate a change in volume

$$(16) \Delta V = \frac{1}{k} \log \frac{P}{P_1} \text{ if } P = P_{1R} \text{ and } P_1 = P_{1R}$$

The latter part of equation (15) ($V_R - V_{1R}$) indicates a change in corneal indentation of $\Delta V_{(R-1R)}$. Equation (15) may therefore be expressed as

$$(17) \Delta V_{(R-1R)} = \Delta V + \Delta V$$

From this equation (17) it is obvious that the change in ocular volume $\Delta V_{(R-1R)}$

method employed for these calculations is identical with the one described above for calculation of the various ΔV_c values. The results obtained are listed in Table III and demonstrated in Fig. 7. An increase in ΔV_c values exists at lower intraocular pressures which was to be expected because of the previously mentioned upward concave slope of the ΔV curve (Fig. 6). The increase in ΔV_c which occurs at $R = 0.3$ may, however, need some explanation. By use of equation (11) ΔV may be calculated for various values of R . Calculating ΔV for R_1 and R the difference will be

$$\begin{aligned}\Delta V_{R_1} - \Delta V_{R_2} &= \frac{1}{K} \log \frac{P_{t_1}}{P_{tR}} + V_{cR_1} - V_{cR_2} \\ &- \left(\frac{1}{K} \log \frac{P_{t_0}}{P_{tR}} + V_{cR} - V_{cR_2} \right) \\ (15) \Delta V_{(R_1-R)} &= \frac{1}{K} \log \frac{P_{tR}}{P_R} + V_{cR} - V_{cR}\end{aligned}$$

Table III
Changes in ocular volume in mm per a plunger deflection (ΔV_c)

R	(Friedenwald)			R	(Langham and Hetland Eriksen)		
	55 g	75 g	10 g		55 g	75 g	10 g
0	0.036	0.040	0.0616	0	0.1510	0.1550	0.1510
1	0.012	0.0616	0.0644	1	0.1310	0.1345	0.1305
2	0.0696	0.0668	0.0632	2	0.1225	0.1195	0.1155
3	0.0688	0.0656	0.0624	3	0.1130	0.1095	0.1055
4	0.0692	0.0652	0.0620	4	0.1050	0.1010	0.0970
5	0.0696	0.0664	0.0632	5	0.1000	0.0955	0.0920
6	0.0708	0.0676	0.0636	6	0.0910	0.0920	0.0885
7	0.0712	0.0692	0.0652	7	0.0950	0.0900	0.0865
8	0.0728	0.0704	0.0668	8	0.0950	0.0890	0.0860
9	0.0744	0.0728	0.0688	9	0.0955	0.0890	0.0860
10	0.0768	0.0744	0.0700	10	0.0910	0.0900	0.0875
11	0.0776	0.0760	0.0728	11	0.0950	0.0910	0.0880
12	0.0800	0.0788	0.0752	12	0.0990	0.0915	0.0885
13	0.0819	0.0820	0.0785	13	0.1000	0.0920	0.0890
14	0.0832	0.0840	0.0812	14	0.1070	0.0930	0.0905
15	0.0810	0.0812	0.0852	15	0.1035	0.0945	0.0970
16	0.0895	0.0892	0.0872	16	0.1050	0.0955	0.0930
17	0.0909	0.0932	0.0900	17	0.1070	0.0970	0.0945
18	0.0950	0.0964	0.0943	18	0.1080	0.0975	0.0955
19	0.0980	0.0976	0.0974	19	0.1090	0.0980	0.0960

$$\Delta V_{(R+R)} = \frac{1}{K} \log \frac{\frac{W}{a+b} \frac{R_1}{R}}{\frac{W}{a+b} \frac{R}{R_1}} + V_R - V_{cR}$$

$$= \frac{1}{K} \log \frac{a+b}{a+b} \frac{R}{R_1} + \Delta V_{(R+R)}$$

The first part of this equation $(\frac{1}{K} \log \frac{a+b}{a+b} \frac{R}{R_1})$ reflects ΔV_e which accordingly is dependent upon variations in R and K alone not in plunger weights

As mentioned above Friedenwald's average normal rigidity coefficient value of 0.0215 is probably too large. Experimental studies by Langham (1963) concerning the pressure volume relationship of the eye yields lower rigidity coefficient values in addition to support the view that the rigidity coefficient demonstrates a significant decrease with increasing intraocular pressure. These findings are confirmed by the experimental data offered by Ytteborg (1960) and Hetland Eriksen (1966). As the P_t values of Friedenwald were based on experimental data and not calculated by use of his rigidity coefficient value of 0.0215 his P_t values are of the same order of magnitude as found by other authors and may be trusted for clinical use. The change in ocular volume (ΔV_e) may accordingly be calculated from Langham's data corresponding to the various levels of intraocular pressure offered by Friedenwald's P_t table for each scale reading. This has been done in Fig. 9. A large difference is noted between the ΔV_e values calculated by use of Langham's data compared with the ΔV_e values calculated through equation (16) by use of Friedenwald's data.

In Fig. 10 the ΔV_e values of Langham is added to the ΔV_t values of Hetland Eriksen (top) and the $\Delta V_{e\mu}$ values of Friedenwald (bottom). The ΔV_e values of Langham - Hetland Eriksen are somewhat larger than Langham - Friedenwald's values because of the previously discussed difference in their ΔV respective ΔV_t values. More important the ΔV_e values of Langham - Hetland Eriksen which are based on equations (5) (6) (7) and listed in Table III are significantly and strikingly larger than the ΔV values based on Friedenwald's data as shown in Fig. 8 and Table III.

In spite of the convenience of using Friedenwald's 1955 tables it seems at present more reasonable to use data which may be confirmed by experimental procedures on human eyes. This is certainly most important when dealing with the ΔV values because of the large difference which exists between Friedenwald's theoretically based figures compared with Langham and Hetland Eriksen's experimentally ones. According to authors opinion therefore the Langham - Hetland Eriksen data should be preferred in the procedure of converting the indentation pulse amplitude in μ plunger deflection into a corresponding

which occurs during tonometry when the plunger moves from R_1 to R_2 is actually composed of two different volumes ΔV_e and ΔV_c . The ΔV_e will reflect the change in ocular volume which corresponds to the difference in intraocular pressure at eye tension level R_1 and R_2 whereas the ΔV_c will reflect the change in corneal indentation which occurs by a plunger displacement from scale reading R_1 to R_2 . If $R_2 = 0.5 + R_1$ and the various volume differences are divided by 25 the ΔV_{μ} , $\Delta V_{e\mu}$ and $\Delta V_{c\mu}$ values are obtained as previously described. This is visualized in Fig 8. At high intraocular pressures ($R = 11.3$) the $\Delta V_{e\mu}$ values are large which explains the increase in ΔV_{μ} values demonstrated above (Fig 7).

It has previously been demonstrated that the ΔV_e and $\Delta V_{c\mu}$ values change with different plunger weights (equations (1) (2) (3) and (5) (6) (7)). The ΔV_e values are not however dependent upon plunger weights. This may be visualized by use of Friedenwald's formula for P_t calculation $\frac{W}{P_t} = a + b R$ i.e. $P_t = \frac{W}{a + b R}$ where W is the weight of the plunger assembly and a and b are constants used at all plunger weights without change of their numerical values. Inserting $\frac{W}{a + b R}$ in equation (15) gives

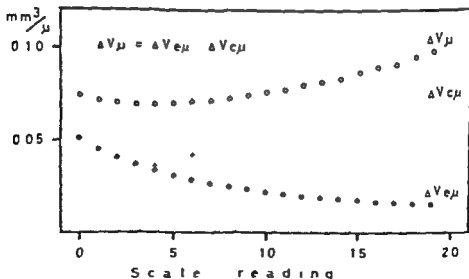


Fig 8

The change in ocular volume in mm³ per μ plunger deflection (ΔV_{μ}) consists of two parameters ΔV_e and $\Delta V_{c\mu}$. The first is most important at higher levels the latter is most important at lower levels of intraocular pressure (Friedenwald's data)

$$\Delta V_{(R-R)} = \frac{1}{k} \log \frac{\frac{W}{a+b} \frac{R_1}{R}}{\frac{W}{a+b} \frac{R_2}{R}} + V_R - V_R$$

$$= \frac{1}{k} \log \frac{a+b}{a+b} \frac{R_2}{R_1} + \Delta V_{(R-R)}$$

The first part of this equation $(\frac{1}{k} \log \frac{a+b}{a+b} \frac{R_2}{R_1})$ reflects ΔV_e which accordingly is dependent upon variations in R and k alone not in plunger weights

As mentioned above Friedenwald's average normal rigidity coefficient value of 0.0215 is probably too large. Experimental studies by Langham (1963) concerning the pressure volume relationship of the eye yields lower rigidity coefficient values in addition to support the view that the rigidity coefficient demonstrates a significant decrease with increasing intraocular pressure. These findings are confirmed by the experimental data offered by Ytteborg (1960) and Hetland Eriksen (1966). As the P_t values of Friedenwald were based on experimental data and not calculated by use of his rigidity coefficient value of 0.0215 his P_t values are of the same order of magnitude as found by other authors and may be trusted for clinical use. The change in ocular volume (ΔV_e) may accordingly be calculated from Langham's data corresponding to the various levels of intraocular pressure offered by Friedenwald's P_t table for each scale reading. This has been done in Fig. 9. A large difference is noted between the ΔV values calculated by use of Langham's data compared with the ΔV_e values calculated through equation (16) by use of Friedenwald's data.

In Fig. 10 the ΔV_e values of Langham is added to the ΔV_{t_e} values of Hetland Eriksen (top) and the ΔV values of Friedenwald (bottom). The ΔV values of Langham - Hetland Eriksen are somewhat larger than Langham - Friedenwald's values because of the previously discussed difference in their ΔV_{t_e} respective ΔV_t values. More important the ΔV_{t_e} values of Langham - Hetland Eriksen which are based on equations (5) (6) (7) and listed in Table III are significantly and strikingly larger than the ΔV values based on Friedenwald's data as shown in Fig. 8 and Table III.

In spite of the convenience of using Friedenwald's 1955 tables it seems at present more reasonable to use data which may be confirmed by experimental procedures on human eyes. This is certainly most important when dealing with the ΔV values because of the large difference which exists between Friedenwald's theoretically based figures compared with Langham and Hetland Eriksen's experimentally ones. According to authors opinion therefore the Langham - Hetland Eriksen data should be preferred in the procedure of converting the indentation pulse amplitude in μ plunger deflection into a corresponding

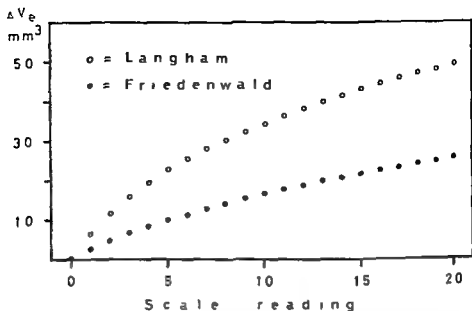


Fig 9

The change in ocular volume (ΔV_e) which occurs when the intraocular pressure falls from 51.4 mm Hg ($P_{IR=0}$) to 14.4 mm Hg ($P_{IR=0}$). Please note the striking difference between Langham's (o) and Friedenwald's (•) data

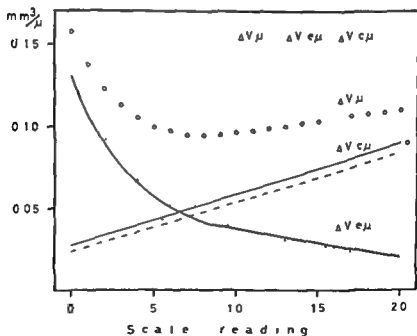


Fig 10

The change in ocular volume in mm^3 per μ plunger deflection (ΔV_μ) which is formed by adding Langham's ΔV_{e_i} data to Hetland Eriksen's ΔV_{t_i} data (o) and to Friedenwald's ΔV_c data (+) (5.5 g plunger weight)

change in ocular volume. This may be visualized by the following example. An indentation pulse of 30 μ amplitude recorded with the 5.5 g plunger weight at $R = 2$ and $R = 8$ will correspond to the following changes in ocular volume:

	Friedenwald	Langham-Hetland-Eriksen
$R = 2$	2 088 mm ³	3 675 mm ³
$R = 8$	2 184 mm ³	2 850 mm ³

Comment

A corneal indentation pulse of a certain amplitude in μ may be converted into mm Hg P values, mm Hg P_t values, mm³ of corneal indentation or mm³ change in ocular volume as described above. The advantage of converting the μ indentation pulse value into one or all of these parameters is stressed by the fact that a certain μ indentation pulse amplitude yields different values of these parameters depending on the eye tension level. As the indentation pulse primarily reflects the change in ocular volume produced by the excess of blood entering the eye at each pulse beat, the most appropriate and practical method of indentation pulse registration should be to convert the μ amplitude into a corresponding change in ocular volume in mm³ by use of Table III. By doing so, it should also be stated whether Friedenwald's or the preferable Langham-Hetland-Eriksen's data are used for this conversion, as these two pairs of converting tables differ markedly from each other.



Summary

The corneal indentation pulse recorded in μ plunger deflection by use of dynamic tonometry reflects changes in the tonometry parameters P_0 , P_t , V_c and ΔV . The present paper supplies formulas and converting tables which should facilitate the procedure of converting the indentation pulse amplitude in μ plunger deflection into one or all of these parameters at all tension levels.

Acknowledgment

The skilful technical assistance of Mrs. Gull Britt Huseby is gratefully acknowledged.

References

- Bron A J Knox D L & Gaasterland D* Tonographic studies in carotid occlusive disease *Brit J Ophthal* 51 577 595 1967
- Eisenlohr J E Langham M E & Maumence A E* Manometric studies of the pressure volume relationship in living and enucleated eyes of individual human subjects *Brit J Ophthal* 46 536 548 1962
- Friedenwald J S* Tonometer calibration An attempt to remove discrepancies found in the 1954 calibration scale for Schiøtz tonometers *Trans Amer Acad Ophthal Otolary* 61 108 123 1957
- Helland Eriksen J* On tonometry 7 The volume of displaced fluid by Schiøtz tonometry *Acta Ophthal (Kbh)* 44 725 736 1966
- Horten I* Dynamic tonometry 1 The dynamic tonometer *Acta Ophthal (Kbh)* 46 1213 1221 1968
- Langham M* A new procedure for the analysis of intraocular dynamics in human subjects *Exp Eye Res* 2 314 324 1963
- Yttborg J* Further investigations of the factors influencing size of rigidity coefficient *Acta Ophthal (Kbh)* 38 643 657 1960

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DYNAMIC TONOMETRY

III The corneal indentation pulse in normal and glaucomatous eyes

BY

IVAR HØRVEN

The corneal indentation pulse has previously been recorded by use of various methods. An electronic tonometer of conventional type was employed by *Danger* (1963) and *Bron et al* (1967). *Bynke & Krakau* (1964) approached the problem by development of a new technique for corneal indentation pulse registration called oculosphygmography. This technique may be handy for clinical comparison of the indentation pulse in the two eyes of the same subject. It suffers the disadvantage however of not offering the possibility of conversion of the recorded pulsations into change in mm Hg intraocular pressure or mm³ ocular volume. This difficulty may be overcome by use of the dynamic tonometer which is an improved standardized Schiøtz electronic tonometer supplied with a zero suppression unit (*Horven 1968 a*) and for which the necessary conversion tables have been provided (*Horven 1970*).

The corneal indentation pulse registration may be of diagnostic interest in various diseases which in one way or another affect the ocular blood supply. Thus a decrease of the indentation pulse have been demonstrated in carotid artery occlusive disease (*Castren & Lavikainen 1964*, *Bynke & Krakau 1964*, *Bynke 1966*, *Bron et al 1967*, *Galín 1967*) following optic glioma resection (*Bynke & Krakau 1964*, *Horven 1965 b*) and in giant cell arteritis (*Horven 1963 c*). A decrease in ocular pulsation have also been demonstrated in luetic

choroidal atrophy (*Suuki* 1962) and tapetoretinal degeneration (*Horven* 1968b). An increase of the indentation pulse amplitude may be present in eyes harboring choroidal melanomas (*Horven* 1969 a) during pain attacks of cluster headache (*Broch et al* 1970) in carotid cavernous fistula (*Boyes & Ralph* 1954, *Horven* 1968 b) and Sturge Weber's disease (*Flage & Horven* 1970).

The known pressure volume relationship of the eye implies that if the increase in ocular blood volume in systole is the same with high as with low intraocular pressure the pulsations in ocular pressure will be greatest when the pressure is high, a formulation offered by *Davanger* (1964). In his studies on ocular pulsation *Davanger* (1963) found that the pulse synchronous changes in intraocular pressure increased with increasing pressure levels. The corresponding indentation pulse amplitude and the mm³ change in ocular volume were however fairly constant at all eye tension levels. *Comberg & Pilz* (1961) measured enlarged indentation pulse amplitudes in eyes with elevated intraocular pressure providing that the pressure elevation was produced by an increase of the venous pressure obtained by insufflation of a neck cuff. If the intraocular pressure was elevated by manual compression of the eye ball no enlargement of amplitudes was found. *Bynke* (1968) on the other hand demonstrated increase of indentation pulse amplitudes by elevated intraocular pressure levels findings which suggest that an increase also exists in mm³ change in ocular volume.

This problem will be dealt with in the present study which main purpose is to evaluate the normal values of corneal indentation pulse amplitudes at various levels of intraocular pressure in normal and glaucomatous eyes.

Material

The present study includes observations in 150 patients with a total of 200 eyes. The material is composed as follows:

Eyes with normal intraocular pressure i.e. with eye tension between Schiotz-scale reading 30 and 10 measured with the 50 g plunger weight

A 100 normal eyes from 100 patients. Age 5-81 years. Sex 61 females 39 males.

B 27 glaucomatous eyes from 27 glaucoma patients. Age 40-80 years. Sex 17 females 10 males. These eyes were all under adequate treatment for glaucoma; a surgical procedure had previously been performed in some of them.

C 65 mate eyes from the above (A) 100 patients. These eyes were either normal or suffered from eye diseases which to our present state of knowledge do not affect the size of the indentation pulse amplitude.

D 13 mate eyes from the above (B) 27 glaucoma patients. These eyes were also under adequate treatment for glaucoma.

Eyes with pathologically increased intraocular pressure : *e* with eye tension between scale reading -1 and 3 measured with the 5.5 g plunger weight

E 45 glaucomatous eyes from 23 glaucoma patients All of these eyes were under heavy but inadequate medical treatment for their glaucoma

Methods

Dynamic tonometry was performed with the 5.5 g plunger weight Following eye tension registration the indentation pulse was recorded with a sensitivity setting of 2 and 1 mV per paper division 1 mV output equals one μ plunger deflection The indentation pulse amplitude in μ plunger deflection was converted into mm^3 change in ocular volume (ΔV) by use of the Langham - Hetland Eriksen data and the pulse-synchronous change in mm Hg intraocular pressure ($\Delta P - \Delta P_0$) were calculated as previously described (Hørvén 1970)

Dynamic tonometry is performed on patients in the supine position just like an ordinary Schiotz tonometry It is of major importance however to keep the tonometer head in the exact vertical position with the plunger resting on the very center of the cornea To avoid sticking of the plunger frequent cleaning is necessary This is especially true when dynamic tonometry is performed on very soft eyes which yield rather small indentation pulse amplitudes

Results

The results obtained by dynamic tonometry examinations are listed in Table 1 In the 100 normal eyes (A) a mean corneal indentation pulse amplitude of 30.02 μ ($\sigma = 10.048$) was obtained Identical values were found in all the other normotensive eye groups (B C D) When all these groups are pooled together (A + B + C + D) a mean indentation pulse amplitude of 29.84 μ ($\sigma = 11.610$) is obtained The 45 hypertensive glaucoma eyes (E) yielded a mean indentation pulse value of 43.09 μ ($\sigma = 17.666$) When these hypertensive glaucoma eyes (E) are tested statistically by application of the Student's *t* test against the normotensive glaucoma eyes (B + D) and against the total number of normotensive eyes (A + B + C + D) a *t* value of 4.338 respective 4.816 was obtained The difference in corneal indentation pulse amplitudes demonstrated between the hypertensive and normotensive eye groups is therefore considered as highly significant ($P < 0.001$)

In order to study in detail the relationship between corneal indentation pulse amplitudes and intraocular pressure the values obtained at various eye tension

choroidal atrophy (Suzuki 1962) and tapetoretinal degeneration (Horven 1968b). An increase of the indentation pulse amplitude may be present in eyes harboring choroidal melanomas (Horven 1969 a) during pain attacks of cluster headache (Broch *et al* 1970) in carotid cavernous fistula (Boyes & Ralph 1954 Horven 1968 b) and Sturge Weber's disease (Flagg & Horven 1970).

The known pressure volume relationship of the eye implies that "if the increase in ocular blood volume in systole is the same with high as with low intraocular pressure the pulsations in ocular pressure will be greatest when the pressure is high" a formulation offered by Davanger (1964). In his studies on ocular pulsation Davanger (1963) found that the pulse synchronous changes in intraocular pressure increased with increasing pressure levels. The corresponding indentation pulse amplitude and the mm^3 change in ocular volume were however fairly constant at all eye tension levels. Comberg & Piltz (1961) measured enlarged indentation pulse amplitudes in eyes with elevated intraocular pressure providing that the pressure elevation was produced by an increase of the venous pressure obtained by insufflation of a neck cuff. If the intraocular pressure was elevated by manual compression of the eye ball no enlargement of amplitudes was found. Bynke (1968) on the other hand demonstrated increase of indentation pulse amplitudes by elevated intraocular pressure levels findings which suggest that an increase also exists in mm^3 change in ocular volume.

This problem will be dealt with in the present study which main purpose is to evaluate the normal values of corneal indentation pulse amplitudes at various levels of intraocular pressure in normal and glaucomatous eyes.

Material

The present study includes observations in 150 patients with a total of 250 eyes. The material is composed as follows:

Eyes with normal intraocular pressure 1 c with eye tension between Schiotz scale reading 30 and 10 measured with the 50 g plunger weight

A 100 normal eyes from 100 patients. Age 5-81 years. Sex 61 females 39 males.

B 27 glaucomatous eyes from 27 glaucoma patients. Age 40-80 years. Sex 17 females 10 males. These eyes were all under adequate treatment for glaucoma a surgical procedure had previously been performed in some of them.

C 65 mate eyes from the above (A) 100 patients. These eyes were either normal or suffered from eye diseases which to our present state of knowledge do not affect the size of the indentation pulse amplitude.

D 13 mate eyes from the above (B) 27 glaucoma patients. These eyes were also under adequate treatment for glaucoma.

levels are listed with half a scale reading intervals in Table II and visualized in Fig 1. Fig 1 demonstrates that the increase in μ indentation pulse amplitudes at higher levels of intraocular pressure is comparatively smaller than the corresponding increase in ΔV and mm Hg (ΔP_o , ΔP_i). The increase which exists in these parameters (ΔV , ΔP_o , ΔP_i) at high intraocular pressure is therefore also highly significant as compared with the corresponding data in normotensive eyes. As will be discussed later, the indentation pulse is dependent on and caused by a pulse-synchronous change in ocular volume. This volume

Table II

The normal corneal indentation pulse values obtained at various eye tension levels as measured with the 55 g plunger weight

Scale reading	Number of eyes N	Corneal indentation pulse recordings				
		μ	σ	ΔV	σ	t value †
10	3	38.7	14.45	3.30	1.18	0.221
9.5	0					
9	1	25.0				
8.5	1	30.0				
8	5	26.8	5.07	2.55	0.43	2.406 x
7.5	7	24.7	4.63	2.35	0.44	3.679 xxx
7	21	26.0	8.55	2.47	0.81	3.064 xx
6.5	22	23.0	10.46	2.69	1.00	1.873
6	37	30.1	7.31	2.97	0.71	
5.5	16	30.6	8.26	3.02	0.81	
5	43	31.8	10.12	3.18	1.01	
4.5	18	29.2	10.06	3.00	1.03	
4	22	33.2	13.31	3.49	1.40	
3.5	1	26.7	5.06	2.91	0.52	
3	11	39.2	16.55	4.43	1.87	2.141 x
2.5	9	47.9	16.31	5.06	1.93	2.843 xx
2	10	43.3	22.30	5.97	2.73	3.124 xx
1.5	3	39.3	16.01	4.84	1.51	2.831 xx
1	4	34.0	9.09			
0.5	3	42.0	20.30			
0	2	34.5	14.85			
-1 ††	3	63.3	13.62	7.40	3.03	3.903 xxx

† Student's t test employed by testing the various results against data obtained at R = 5

†† Converting values employed as for R = 0

Table I
Composition of material and results obtained in various groups of patients

Patient group	Number of eyes N	Mean intraocular pressure (mm Hg)		Amplitude (mean) μ	Standard deviation σ	Mean amplitude converted into		
		P_o	P_t			(mm^2) ΔV	(mm Hg) ΔP_o	(mm Hg) ΔP_t
A	100	15.1	29.4	30.02	10.048			
B	27	18.4	32.1	29.85	9.746			
C	65	15.1	29.4	29.59	9.139			
D	13	19.5	33.1	29.69	9.223			
A+B+C+D	205	15.8	30.0	29.84	9.610	2.96	1.49	1.92
E	45	30.0	41.8	43.09	17.666	5.48	4.34	3.66

levels are listed with half μ scale reading intervals in Table II and visualized in Fig 1. Fig 1 demonstrates that the increase in μ indentation pulse amplitude at higher levels of intraocular pressure is comparatively smaller than the corresponding increase in mm^3 (ΔV) and mm Hg (ΔP_o , ΔP_i). The increase which exists in these parameters (ΔV , ΔP_o , ΔP_i) at high intraocular pressure is therefore also highly significant as compared with the corresponding data in normotensive eyes. As will be discussed later, the indentation pulse is dependent on and caused by a pulse-synchronous change in ocular volume. This volume

Table II

The normal corneal indentation pulse values obtained at various eye tension levels as measured with the 5.5 g plunger weight

Scale reading	Number of eyes N	Corneal indentation pulse recordings				
		μ	σ	ΔV	σ	t value †
10	3	33.7	14.45	3.30	1.18	0.221
9.5	0					
9	1	25.0				
8.5	1	30.0				
8	5	26.8	5.07	2.55	0.43	2.406 x
7.5	7	24.7	4.63	2.35	0.44	3.679 xxx
7	21	26.0	8.55	2.47	0.81	3.064 xx
6.5	22	28.0	10.46	2.69	1.00	1.873
6	37	30.1	7.31	2.97	0.71	
5	16	30.6	8.96	3.07	0.81	
4.5	45	31.8	10.12	3.18	1.01	
4	38	29.9	10.06	3.00	1.03	
3.5	7	33.2	13.31	3.49	1.40	
3	11	26.7	5.06	2.91	0.55	
2.5	9	119.9	16.55	4.43	1.87	2.141 x
	10	49.9	16.37	3.06	1.93	2.843 xx
1.5	3	43.3	22.30	5.97	2.73	3.174 xx
1	4	39.3	16.04	4.84	1.51	2.831 xx
0.5	3	34.0	9.09			
0	3	42.0	20.30	7.40	3.03	3.903 xxx
-1 ††	3	34.5	14.85			
		63.3	13.63			

† Student's t test employed by testing the various results against data obtained at $R = 5$

†† Converting values employed as for $R = 0$

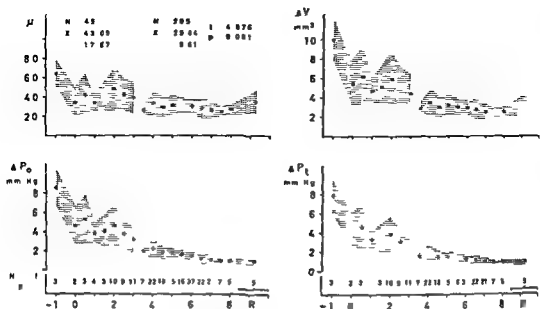


Fig 1

Corneal indentation pulse values obtained in μ , ΔV , ΔP_0 and ΔP_i at various eye tension levels as measured with the 5.5 g plunger weight in 250 human eyes
Shaded area = mean $\pm 1 \sigma$

has been calculated at half a scale reading intervals and is listed in Table II. The change in mm^3 pulsatile volume (ΔV) obtained at various scale readings was compared with the value obtained at scale reading 5 ($\Delta V_{R=5}$) by use of the Student's t test. The various significance levels ($\alpha = 5\%$, $\alpha\alpha = 1\%$, $\alpha\alpha\alpha = 0.1\%$) is indicated in Table II by use of the symbol α adjacent to the listed t values. As demonstrated a marked and significant increase of the pulsesynchronous change in ocular volume exists at an elevated intraocular pressure level of 37.57 mm Hg ($P_{iR=5} - P_{iR=1}$). A less striking but still significant decrease in pulsatile volume exists at $R = 7 - R = 8$.

The following conclusions may be drawn. The corneal indentation pulse amplitude in microns of plunger movement is dependent on the eye tension level and will to some extent increase with decreasing values of R when the 5.5 g plunger weight is employed. The corresponding pulsesynchronous variation in ocular volume will change in a fairly identical pattern. The pulsesynchronous changes in intraocular pressure (ΔP_0 and ΔP_i) demonstrate a growing mm Hg increase with increasing levels of intraocular pressure (Fig 1). This increase is more pronounced than the increase in mm^3 pulsatile volume, a fact which is fully explained by the known pressure-volume relationship of the eye as previously discussed.

The present material offers possibilities of further information

Age distribution The corneal indentation pulse amplitudes in microns of plunger movement are plotted against the age of the 127 patients with normotensive eyes (A + B) and listed in Table III. As demonstrated the indentation pulse amplitudes are of the same order of magnitude in subjects below 60 years of age. At higher age a slight decrease in corneal indentation pulse amplitudes exists which probably reflects the more rigid arteries and arterioles in that age group compared with those of younger subjects. The decrease is significant at the 1% level as judged by the Students *t* test.

Sex distribution The present material (A + B) consists of 78 females and 49 males. A mean corneal indentation pulse amplitude of 31.4μ ($\sigma = 9.587$) was obtained in the females compared with 27.7μ ($\sigma = 10.184$) in the males. This difference is significant at the 5% level as judged by the Students *t* test. No proper explanation of this fact is offered. The difference in amplitudes between the two sexes is accepted with some reservations as the material was not primarily selected in order to study the sex relationship. Thus the material contains 61.4% females and 38.6% males instead of the more preferable 50% of each group.

The consistency of the recordings was studied in 33 patients (57 eyes) which were examined twice at various intervals from one day to several months. The results are presented in Fig. 2 which gives the amplitudes in microns of plunger movement of the first (x = abscissa) and the second (y = ordinate) examinations. There is a definite correlation between the results of the two examinations fitting the equation $y = 4.3894 + 0.8744 x$. A correlation coefficient of $r = 0.8005$ was obtained indicating a highly significant correlation between x and y ($t = 6.635$, $P < 0.001$). The various x values were also tested against the corresponding y values by use of the statistical method of paired comparison. No significant difference between the x and y values of the same subject was demonstrated ($t = 1.47$). Accordingly the indentation pulse amplitude may be regarded as a rather constant and characteristic value in the one subject although large variations in amplitudes exist between the different subjects.

Right eye - left eye comparison Fig. 3 offers the corneal indentation pulse amplitude of the right eye (x = abscissa) plotted against the left eye value (y = ordinate) in 34 subjects which yielded identical and normal eye tension readings in their two eyes. The data obtained fits the equation $y = 0.1935 + 0.9913 x$ ($r = 0.997$). No significant difference between the two eyes of the same subject was demonstrated.

Normotensive eyes with small differences in eye tension levels 31 subjects demonstrated a mean difference of $R = 0.73$ in eye tension between their two eyes i.e. a difference of 1.51 mm Hg intraocular pressure (P_1 values $\bar{x} = 29.951$, $y = 28.438$ mm Hg). Plotting the corneal indentation pulse amplitude from the eye with higher intraocular pressure (x = abscissa) against the eye

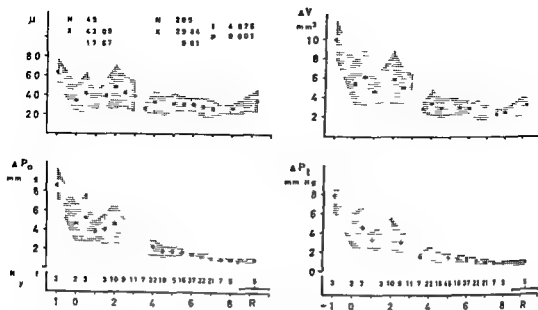


Fig 1

Corneal indentation pulse values obtained in μ , ΔV , ΔP_0 and ΔP_t at various eye tension levels as measured with the 5.5 g plunger weight in 200 human eyes
Shaded area = mean $\pm 1 \sigma$

has been calculated at half γ scale reading intervals and is listed in Table II. The change in mm³ pulsatile volume (ΔV) obtained at various scale readings was compared with the value obtained at scale reading 5 ($\Delta V_{R=5}$) by use of the Student's t test. The various significance levels ($\alpha = 5\%$, $\alpha\alpha = 1\%$, $\alpha\alpha\alpha = 0.1\%$) is indicated in Table II by use of the symbol α adjacent to the listed t values. As demonstrated a marked and significant increase of the pulsesynchronous change in ocular volume exists at an elevated intraocular pressure level of 37.57 mm Hg ($P_{(R=5)} - P_{(R=1)}$). A less striking but still significant decrease in pulsatile volume exists at $R = 7 - R = 8$.

The following conclusions may be drawn. The corneal indentation pulse amplitude in microns of plunger movement is dependent on the eye tension level and will to some extent increase with decreasing values of R when the 5.5 g plunger weight is employed. The corresponding pulsesynchronous variation in ocular volume will change in a fairly identical pattern. The pulsesynchronous changes in intraocular pressure (ΔP_0 and ΔP_t) demonstrate a growing mm Hg increase with increasing levels of intraocular pressure (Fig 1). This increase is more pronounced than the increase in mm³ pulsatile volume a fact which is fully explained by the known pressure volume relationship of the eye as previously discussed.

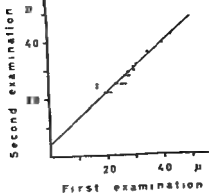


Fig 2

Consistency of corneal indentation pulse recordings obtained by examination of 57 eyes at intervals from 1 day to several months

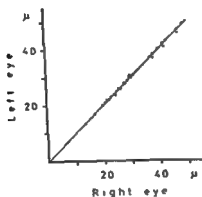


Fig 3

Corneal indentation pulse registration in right and left eye in 34 subjects

with lower intraocular pressure (y = ordinate) yields data fitting the equation $y = 1.352 + 0.921x$ ($r = 0.984$). The results are visualized in Fig 4. In the eyes with lower intraocular pressure the amplitudes were larger in 3 eyes of equal size in 13 and lower in 15 eyes which indicates that a slight reduction of the corneal indentation pulse amplitudes should be expected in the eye with lower intraocular pressure. In the 31 subjects above yielding differences in eye tension between their two eyes of 1 mm scale readings or less this difference in

Table III
Corneal indentation pulse amplitudes in relation to age

Age	<10	10	20	30	40	50	60	70	80
N	2	7	12	10	21	33	22	16	80
\bar{x}	20.50	32.14	31.33	29.70	31.05	32.98	27.86	26.50	24.00
σ	0.71	10.57	10.29	10.11	10.20	12.03	7.61	7.07	3.27
N									
x	21			64			42		
σ	30.57			31.78			26.98		
	10.16			11.07			7.08		
				$t = 0.463$			$t = 2.720 \text{ xx}$		

N = number of patients \bar{x} = mean corneal indentation pulse amplitude in μ σ = standard deviation

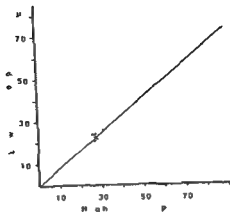


Fig 5

Corneal indentation pulse recordings in 27 glaucoma patients with a pronounced difference in eye tension between their two eyes

pressure (x = abscissa) was plotted against the amplitude of the eye with lower intraocular pressure (y = ordinate) and the results are presented in Fig 5. The data obtained fitted the equation $y = -0.487 + 0.835 x$ ($r = 0.94$) which indicates that an average reduction in amplitude of about 17% exists in the eyes with lower intraocular pressure of these 27 glaucoma patients. This difference in corneal indentation pulse amplitude between the two eyes in the same subject is highly significant ($P < 0.001$) as judged by the Wilcoxon Signed ranks test and confirms the results presented in Table II and discussed above.

Comparison of amplitudes recorded in the same eye at various eye tension levels. In order to study the possible difference in corneal indentation pulse amplitudes in normotensive eyes with differences in eye tension exceeding 2 scale readings Schiotz tonography was performed in 15 normal eyes (14 subjects). By use of the calibrated zero suppression equipment of our Mark 280 recorder the tracings may be kept on the running paper even when the sensitivity is increased as demonstrated in Fig 6. Accordingly the corneal indentation pulse amplitudes may be measured with sufficient degree of accuracy at the start and end point of the tonography procedure. The results obtained are presented in Table IV. The average intraocular pressure in the 15 eyes was 30.14 mm Hg (P_i) at start and 25.08 mm Hg (P_e) at the end of tonography. A highly significant decrease was demonstrated in corneal indentation pulse amplitudes and in pulse-synchronous change in ocular volume (ΔV) as judged by the statistical method of paired comparison. Accordingly during tonography not only will the corneal indentation pulse demonstrate a significant reduction in ampli-

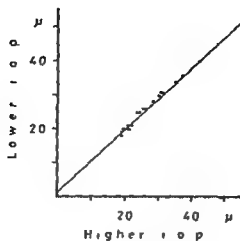


Fig 4

Corneal indentation pulse recordings in 31 subjects with different eye tension levels in their normotensive eyes

amplitude was significant at the 1% level as judged by the Wilcoxon Signed ranks test

Normally therefore a certain difference in corneal indentation pulse amplitude between the two eyes of the same subject may be expected because a difference in eye tension of up to 2 scale readings Schiotz may exist. In order to evaluate the magnitude of this difference in amplitudes between the two eyes in the same subject the 65 subjects mentioned above (C) which had both of their eyes examined were studied in detail. The difference in amplitude between the two eyes was recorded in per cent positive values indicate larger amplitude of right eye negative values indicate larger amplitude of left eye. The differences yielded a normal frequency distribution and varied between -8.51 and +16.67% with an arithmetical mean of $\bar{x} = +1.20\%$ (σ (of population) = 4.61). This indicates that only 0.27% of the population will yield differences beyond $\bar{x} \pm 3\sigma$ i.e. beyond -12.63 and +15.03%. Accordingly the corneal indentation pulse amplitudes are of a similar order of magnitude in the two eyes of the same subject a repeated difference of $\pm 15\%$ or more is considered as a definite pathological finding.

Glaucomatous eyes with larger differences in eye tension levels Most probably a significant difference in amplitudes may be demonstrated between the two eyes also when a more pronounced and pathological difference exists between their intraocular pressures. 27 glaucoma patients demonstrated a mean difference in intraocular pressure of 6.74 mm Hg (P_t values $\bar{x} = 41.088$, $\bar{y} = 34.345$) i.e. a mean difference in eye tension of $N = 1.91$ between their two eyes. The corneal indentation pulse amplitude of the eye with larger intraocular

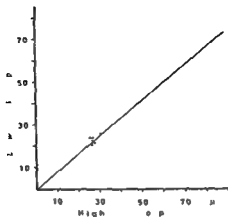


Fig 5

Corneal indentation pulse recordings in 27 glaucoma patients with a pronounced difference in eye tension between their two eyes

pressure (x = abscissa) was plotted against the amplitude of the eye with lower intraocular pressure (y = ordinate) and the results are presented in Fig 5. The data obtained fitted the equation $y = -0.487 + 0.835 x$ ($r = 0.94$) which indicates that an average reduction in amplitude of about 17% exists in the eyes with lower intraocular pressure of these 27 glaucoma patients. This difference in corneal indentation pulse amplitude between the two eyes in the same subject is highly significant ($P < 0.001$) as judged by the Wilcoxon Signed ranks test and confirms the results presented in Table II and discussed above.

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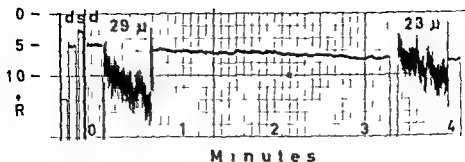


Fig 6

Corneal indentation pulse recordings during tonography

tude the pulsesynchronous change in ocular volume will also decrease along with decreasing intraocular pressure

Indentation pulse amplitudes at higher levels of intraocular pressure This problem was studied in some patients not listed above. The corneal indentation pulse was studied at various eye tension levels by use of the 5.5 and 10 g plunger weights during the period of treatment of 3 patients suffering from acute glaucoma. Although the results were not identical in all cases a definite tendency was recognized. At high intraocular pressures ($P_i = 70-90$ mm Hg) rather small indentation pulse amplitudes were recorded. The amplitudes increased however with decreasing intraocular pressure until a maximum value was obtained at 40-50 mm Hg (P_i). At lower intraocular pressures a marked decrease was found.

The corneal indentation pulse was also examined in a female patient suffering from secondary glaucoma in her left eye caused by lens luxation into the anterior chamber. The corneal indentation pulse amplitude was zero at an intraocular pressure of 93.4 mm Hg (P_i). Following lens extraction with subsequent decrease in intraocular pressure the amplitudes recovered to subnormal values although the eye was amaurotic.

The indentation pulse amplitude pattern evaluated in these patients may not however reflect the pattern in normal eyes as the disease itself may have influenced the blood supply to the eye. The indentation pulse should therefore be recorded at short intervals at different intraocular pressure levels in the same patient. This was obtained in two ways.

First the indentation pulse amplitudes were recorded with the 5.5 and 10 g plunger weight in the same eye. This was done in 90 eyes and the results are presented in Table V. At lower intraocular pressure levels the amplitudes are slightly larger when recorded with the 10 g plunger weight; the difference is not however statistically significant. At higher intraocular pressure levels the amplitudes obtained with the 10 g plunger weight are considerably decreased.

Table IV
 Average values obtained by tonography in 15 eyes. A highly significant decrease in corneal indentation pulse amplitude (intraocular pressure and pulse synchronous change in ocular volume (IV) is observed

Scale reading (R)		Amplitude (μ)		Intraocular pressure (mm Hg)		(mm ³)	
Start	End	Start	End	Start	End	Start	End
4.77	8.50	06.15	07.13	30.14	25.00	2.015	0.131
		$P < 0.001$		$P < 0.001$		$P < 0.001$	
						Difference	
						0.484	
						$P < 0.001$	

Table I

Corneal indentation pulse recorded with 5.5 g and 10 g plunger weights at various eye tension levels (N = number of eyes \bar{R} = scale reading Schiotz (mean) \bar{x} = indentation pulse amplitude in μ (mean))

N	2	4	5	10	8	19	13	16	10	2	1
$R_{5.5}$	1	0	1	2	3	4	5	6	7	8	9
R_{10}	35	49	6	68	79	88	96	109	116	128	135
$\bar{x}_{5.5}$	45.5	37.5	42.5	40.7	32.9	29.9	31.2	34.8	27.0	32.5	24.0
\bar{x}_{10}	27.0	26.5	34.4	40.6	32.0	29.5	33.0	35.9	26.9	33.5	25.0
$\bar{x}_{5.5} - \bar{x}_{10}$	18.5	10.7	8.4	0.1	0.9	0.1	-1.8	-1.1	0.1	-1.0	-1.0

N	11
$\bar{x}_{5.5}$	41.363
\bar{x}_{10}	30.272
$\bar{x}_{5.5} - \bar{x}_{10}$	11.091
t value	2.501 $\alpha\alpha$



Fig. 1

Corneal indentation pulse amplitudes recorded with 5.5 g and 10 g plunger weights. A decrease in amplitude is demonstrated in right eye when the 10 g plunger weight is employed

as shown in Fig. 7. This difference between the 5.5 g and 10 g recordings is significant at the 1% level as judged by the Student's *t* test.

Second, the indentation pulse was recorded in a choroidal melanoma eye at various levels of intraocular pressure obtained by injection of 0.9% saline into the anterior chamber followed by subsequent aspiration of fluid. The experiment was performed under topical anesthesia (oxibuprocaine). The indentation pulse amplitudes obtained at various levels of intraocular pressure (P_i) are visualized in Fig. 8 and Fig. 9. In the latter the corresponding pulse synchronous

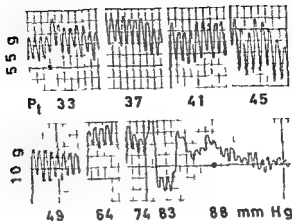


Fig 8

Corneal indentation pulse recorded at various levels of intraocular pressure (P_i) in a canulated melanoma eye. Sensitivity $2 \text{ mV} = 2 \mu$ per paper division

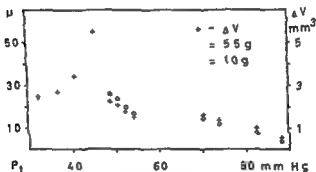


Fig 9

Corneal indentation pulse values in μ plunger movements and mm^3 change in intraocular volume demonstrated at various levels of intraocular pressure in a canulated melanoma eye

change in ocular volume is also given. The results of this experiment confirm in every way what has been found by dynamic tonometry in the clinical material presented above.

Table V

Corneal indentation pulse recorded with 5.5 g and 10 g plunger weights at various eye tension levels (N = number of eyes \bar{R} = scale reading Schiotz (mean) \bar{x} = indentation pulse amplitude in μ (mean))

N	2	4	5	10	8	19	13	16	10	2	1
$R_{5.5}$	-1	0	1	2	3	4	5	6	7	8	9
R_{10}	3.5	4.9	6	6.8	7.9	8.8	9.6	10.9	11.6	12.8	13.5
$\bar{x}_{5.5}$	45.5	31.5	42.5	40.1	32.9	29.9	31.2	34.8	27.0	37.5	24.0
\bar{x}_{10}	27.0	26.5	34.4	40.6	32.0	29.5	33.0	35.9	26.9	33.5	25.0
$\bar{x}_{5.5} - \bar{x}_{10}$	18.5	10.7	5.4	0.1	0.9	0.1	-1.8	-1.1	0.1	-1.0	-1.0

N	11
$\bar{x}_{5.5}$	41.363
\bar{x}_{10}	30.272
$\bar{x}_{5.5} - \bar{x}_{10}$	11.091
t value	2.301 xx



Fig 7

Corneal indentation pulse amplitudes recorded with 5.5 g and 10 g plunger weights. A decrease in amplitude is demonstrated in right eye when the 10 g plunger weight is employed

as shown in Fig 7. This difference between the 5.5 g and 10 g recordings is significant at the 1% level as judged by the Student's t test.

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pulse amplitude. The amplitudes will change corresponding to the various levels of intraocular pressure whether the eye is glaucomatous or not. Accordingly adequately treated glaucomatous eyes with intraocular pressure within normal range will yield normal sized corneal indentation pulse amplitudes. And normal eyes examined during artificial elevation of intraocular pressure will yield an increase in corneal pulse amplitude which may be compared with the increase observed in hypertensive glaucomatous eyes.

As known a certain pulsation in venous pressure exists in the jugular vein being initiated from the right auricle. Compared with the pulse-synchronous change in mm Hg intraarterial pressure this venous pulsation is negligible. Accordingly the bulk of fluid (blood, aqueous humor) which leaves the eye during the systole and diastole will do so at a rather constant speed. The blood will however enter the eye mainly during the systole and only to a much lesser extent during the diastole. When the bulk of blood which enters the eye during diastole (D) is subtracted from the bulk of blood entering the eye in systole (S) the difference ($S - D$) may be called the excess of blood which enters the eye during systole. This volume ($\Delta V = S - D$) will initiate the pulsation in intraocular pressure and may be calculated from the recorded corneal indentation pulse amplitude in microns of plunger movement by use of the conversion table previously presented (Horten 1940). It is stressed that the corneal indentation pulse will reflect the excess of blood entering the eye in systole ($S - D$) and not the bulk of blood which flows through the eye during one heart cycle ($S + D$). Accordingly true values of the bulk of blood which flows through the eye during one heart cycle may be obtained only under the prerequisite that D is zero, a situation which possibly exists when the intraocular pressure equals the diastolic blood pressure of the ophthalmic artery. If the intraocular pressure exceeds the diastolic blood pressure, blood may enter the eye in systole and to some extent return to the ophthalmic artery in diastole, in which case D will be negative. Under these circumstances the bulk of blood which flows through the eye will be less than expected from the indentation pulse recordings as the negative D will participate with S in initiating the pulsations in intraocular pressure. Theoretically therefore if the intraocular pressure and the peripheral vascular resistance were very high, most of the blood entering the eye in systole would not be able to pass into the capillaries and veins. On the contrary a backflow of blood would exist forcing the blood into the ophthalmic artery again. Thus at high levels of intraocular pressure a fair corneal indentation pulse amplitude may be recorded as a consequence of this forward backwards movement of blood in the arterioles while the bulk of blood flowing through the capillaries and veins and supporting the nourishment of the eye may be rather negligible and insufficient. This view was recently supported by experimental studies in farm pigs (Dollery et al 1963). By use of cine fluorescence angiograms a substantial backflow of blood in the retinal arterioles in

Discussion

The results obtained demonstrate that the corneal indentation pulse amplitudes in microns of plunger movement are related to the intraocular pressure level. In normotensive eyes (P_i average 30.07 mm Hg) the mean pulse-synchronous change in indentation pulse amplitude was 29.84 μ which corresponds to a change in ΔV of 2.96 mm³ in ΔP_i of 1.32 mm Hg and in ΔP_o of 1.49 mm Hg. In hypertensive eyes these values were significantly increased. In one of their normal cases *Bron et al* (1967) offer a ΔV value of 2.1 mm³. This value was calculated by use of *Iriedenwald's* data which yields results of about 70% of the *Langham-Hetland-Eriksen* conversion table used in the present study. If *Bron et al* (1967) had employed the conversion table used in this study a ΔV value of 3.0 mm³ would have been demonstrated which actually is identical with the mean value of 2.96 mm³ obtained in the present study. The reason why *Langham-Hetland-Eriksen's* data are preferred for conversion of corneal indentation pulse amplitudes in microns into corresponding mm³ change in ocular volume is discussed in detail elsewhere (*Horven* 1970).

Lawrence & Schlegel (1966) demonstrated in rabbits a ΔV value of 0.407 mm³ which did not change with the intraocular pressure level. The corresponding pulse-synchronous change in intraocular pressure varied between 0.2 mm Hg (normotensive eyes) and 2.0 mm Hg (hypertensive eyes). Identical results were presented by *Bynke* (1968). Thus the values reported from rabbits are only 20-30% of those obtained in man. This discrepancy is probably not caused by the difference in species but by the fact that these animals were examined under general anesthesia. In man the indentation pulse amplitudes and the corresponding changes in ocular volume are reduced to about 30% of their normal values during general anesthesia (*Horven & Syrdalen* 1970) and preliminary experiments on rabbits are confirmative with this observation (*Horven* 1968b). Results concerning the pulse-synchronous change in intraocular pressure and volume obtained in animals (and man) during general anesthesia should therefore be accepted with a large part of skepticism. Such results will not reflect the normal state of non-anesthetized animals. As mentioned above the indentation pulse amplitude reaches its maximum at an elevated intraocular pressure of 37.57 mm Hg. At higher intraocular pressures the amplitudes decrease until zero values when the intraocular pressure exceeds the systolic pressure of the ophthalmic artery. This pattern of indentation pulse amplitude behavior was demonstrated in acute glaucoma, chronic simple glaucoma and capsular glaucoma eyes as well as in eyes with normal outlet channels for the aqueous humor. In these latter eyes the elevated intraocular pressure was obtained either experimentally by injection of fluid into the eye or by a luxated lens which temporarily blocked the chamber fluid drainage. The following conclusions may be drawn: the glaucomatous disease per se does not alter the corneal indentation

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Summary

Corneal indentation pulse registrations have been performed by use of dynamic tonometry in 205 normotensive and 45 hypertensive human eyes. In addition to evaluate the age and sex distribution the normal values of indentation pulse amplitudes are given at various eye tension levels. Normally the indentation pulse amplitudes are of the same order of magnitude in the two eyes of the same subject a difference of $\pm 15\%$ or more between the two eyes is considered as a definite pathological finding.

Acknowledgment

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References

- Bill A. Intraocular pressure and blood flow through the uvea. *A.M.A. Arch. Ophthalmol.* 6: 336-349, 1967.
- Bates I. L. & Polph F. T. Carotid cavernous fistula. *Amer. J. Ophthalmol.* 3: 267-266, 1944.
- Braut I. A. D. Glicker J. & Creates D. F. Photoelectric method of investigating the amount and oxygenation of blood in the fundus oculi. *Brit. J. Ophthalmol.* 45: 161-18, 1961.
- Brich I. et al. Studies on cerebral and ocular circulation in a patient with cluster headache. *Headache* 1970 in press.
- Prin A. J. Knapp D. L. & Gaaierland D. Tonographic studies in carotid occlusive disease. *Brit. J. Ophthalmol.* 51: 5: 393, 1966.
- Pynke H. C. & Krakau C. E. T. A handy instrument for oculo-sphygmography with some clinical results. *Ophthalmologica* 145: 367-373, 1964.
- Rinke H. C. Screening diagnosis of carotid occlusion by means of oculosphygmography. *Neur. J.* 16: 383-391, 1965.
- Rinke H. C. Influence of intraocular pressure on the amplitude of the corneal pulse. A study in man and rabbits. *Acta Ophthalmol. (Kbh.)* 46: 1135-1143, 1968.
- Smith J. A. & Laakkonen P. New method of diagnosing carotid diseases. *Acta Ophthalmol. (Kbh.)* 4: 219-3, 1964.
- Smith G. D. & P. I. A. Augeninnendruck und Rigiditäts erhalten bei experimenteller Augenndruckerhöhung. *Acta Ophthalmol. (Kbh.)* 46: 1139-1147, 1968.
- Smith G. D. & P. I. D. Hemodynamic of large and small vessels in peripheral vascular disease. *Circulation* 34: 453-464.
- Strand M. Studier av de pulsvisnärne i ögontryck. *Norsk Oftalmologisk Tidsskrift* 1969.

diastole was demonstrated. Experimental studies demonstrate also that an artificial elevation of intraocular pressure will cause a reduction in the amount of blood in the choroid (Broadfoot *et al* 1961) and a reduced rate of blood flow through the uvea (Bill 1962).

Of course if the intraocular pressure exceeds the systolic pressure in the ophthalmic artery no blood will enter the eye the indentation pulse amplitude will be zero and the eye will turn amaurotic as demonstrated above in the case with luxated lens. A zero indentation pulse amplitude may however also be recorded when a certain and presumably sufficient bulk of blood flows through the vascular bed of the eye if this blood flow is non pulsatile, i.e. if $S = D$. Clinically this has been observed in two conditions. During general anaesthesia a zero indentation pulse amplitude has been recorded in both eyes of one patient (Horven & Syrdalen 1970). In giant cell arteritis a zero or close to zero indentation pulse amplitude has been recorded by several occasions in eyes with normal or only slightly reduced vision (Horven 1969 b). This latter observation is in complete agreement with the findings of Conrad & Green (1964). They demonstrated that the ratio of flow to pulse was markedly elevated in patients with peripheral arterial occlusive disease. In normotensive eyes the blood most probably flows continuously into the eye in diastole yielding a positive D . If so the bulk of blood which flows through the vascular bed of the eye will exceed the mm^3 change in ocular volume calculated from the recorded indentation pulse amplitude. Thus counting 72 heart beats in a minute the blood flow through the average normal human eye should exceed 0.213 ml per minute (i.e. 2.96 mm^3).

In order to explain the change in magnitude of the indentation pulse amplitude and ΔV which exists at various levels of intraocular pressure it is easily understood that a decrease should occur with increasing intraocular pressure at high levels of intraocular pressure because less blood will enter the eye during these circumstances. More difficult to explain is the fact that a maximum value exists at 37-57 mm Hg intraocular pressure below this level a decrease in amplitude and ΔV occurs with decreasing intraocular pressure as demonstrated above. One possible explanation may be that the pulsatile vascular bed increases with increasing intraocular pressures up to a level of 37-57 mm Hg. Whether the increase in pulsatile vascular bed is initiated by opening of shunts or by stretching of the eye wall and longitudinal extension of the arterioles is unknown. It is known however that in pathological conditions as choroidal melanomas (Horven 1969 a) and Sturge Weber's disease (Flage & Horven 1970) where the pulsatile uveal vascular bed is increased a corresponding increase is obtained also in the corneal indentation pulse amplitude.

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Corneal indentation pulse registrations have been performed by use of dynamic tonometry in 205 normotensive and 45 hypertensive human eyes. In addition to evaluate the age and sex distribution the normal values of indentation pulse amplitudes are given at various eye tension levels. Normally the indentation pulse amplitudes are of the same order of magnitude in the two eyes of the same subject; a difference of $\pm 15\%$ or more between the two eyes is considered as a definite pathological finding.

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References

- Bill A. Intra-ocular pressure and blood flow through the uvea. *N M A Arch Ophthalmol* 6: 336-342, 1967.
- Byes T L & Ralph F T. Carotid cavernous fistula. *Amer J Ophthalmol* 3: 1967: 266-1974.
- Goodfellow H D, Gierster J C, Creates D F. Photoelectric method of investigating the amount and oxygenation of blood in the fundus oculi. *Brit J Ophthalmol* 4: 161-174, 1961.
- Brick A et al. Studies on cerebral and ocular circulation in a patient with cluster headache. *Headache* 1970 in press.
- Fern A J, Knox D L & Caasterland D. Tonographic studies in carotid occlusive disease. *Brit J Ophthalmol* 15: 159, 1967.
- Fynke H C & Kraker C E T. A preliminary report for oculosphygmography with some clinical results. *Ophthalmologica* 145: 367-373, 1964.
- Fynke H C. Screening diagnosis of carotid occlusion by means of oculosphygmography. *Norlitt* 355: 331, 1966.
- Fynke H C. Influence of intra-ocular pressure on the amplitude of the corneal pulse. *Acta Ophthalmologica (Kbh)* 46: 1135-1145, 1968.
- Gustafson J A & Larikainen P. New method of diagnosing carotid diseases. *Acta Ophthalmologica (Kbh)* 42: 19-23, 1964.
- Hamberg D & Fildes A. Augeninnendruck und Blutflussverhalten bei experimenteller Venenstauung. *Arch f Ophthalmol* 103: 189-200, 1961.
- Henriksen M E & Cullen H D. Hemodynamics of large and small vessels in peripheral arterial disease. *Circulation* 7: 34-53, 1964.
- Hansen M. Støtelse ved pulssynke hos svangne og øyets trykk. *Norsk Oftalmologisk Tidsskrift* Nr 4, 1968.

- Davanger M* The ocular pressure and hydrodynamics of the aqueous fluid as illustrated by a mechanical model *Acta Ophthalm (kbb)* 42 735 752 1964
- Dollery C T Henkind P Kohner E M & Paterson J W* Effect of raised intraocular pressure on the retinal and choroidal circulation *Invest Ophthalm* 7 291 298 1968
- Flage T & Horven I* Corneal indentation pulse in Sturge Weber's disease A case report *Acta Ophthalm (kbb)* to be published 1970
- Galin M A Rodrigue Barrion R Pola P & McLean J M* Cerebrovascular insufficiency *Trans Amer Acad Ophthalm Otolaryng* 71 119 125 1967
- Horven I* Dynamic tonometry I The dynamic tonometer *Acta Ophthalm (kbb)* 46 1213 1221 1968 a
- Horven I* Personal observation 1968 b
- Horven I* Dynamic tonometry and giant cell arteritis Comment upon Systemic vascular disease The William Mackenzie Centenary Symposium Glasgow Scotland Sept 24 1968 c
- Horven I* Dynamic tonometry and choroidal melanoma A new diagnostic approach A M A Arch Ophthalm 82 440 445 1969 a
- Horven I* Dynamisk tonometri ved arteritis temporalis VII Nordiske Oftalmologmøte Bergen Norway June 20 1969 b
- Horven I* Dynamic tonometry II Methods of corneal indentation pulse registration *Acta Ophthalm (kbb)* 48 28 38 1970
- Horven I & Syrdalen P* Corneal indentation pulse and general anesthesia *Acta Ophthalm (kbb)* 48 59 66 1970
- Lawrence C & Schlegel W A* Ophthalmic pulse studies I Influence of intraocular pressure *Invest Ophthalm* 5 515 525 1966

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CORNEAL INDENTATION PULSE AND GENERAL ANESTHESIA

BY

IVAR HØRVEN and PER SYRDALEN

Most of the experimental work previously done in animals in order to study the ocular blood supply and hydrodynamics has been performed during general anesthesia. It is quite possible however that the general anesthesia itself to some extent may influence the various factors responsible for the ocular blood supply such as blood pressure, intraocular pressure and the peripheral vascular resistance. In order to investigate this possibility dynamic tonometry (Hørvén 1969) was performed during Nembutal (pentobarbital sodium) anesthesia on two rabbits by one of us (I. H.) with a corneal pulse amplitude recorded close to zero as a result.

This preliminary finding initiated the present study which offers the results obtained by dynamic tonometry performed before following premedication and during general anesthesia in human beings.

Material

The material consists of 24 patients suffering from various eye diseases: (1) strabism (11), retinal detachment (6), glaucoma (7), choroidal melanoma (2), extra

ocular tumors (2) and ptosis (1). The normal mate eye was studied and when possible the affected eye was also included yielding a total of 39 eyes. The age of the patients averaged 27 years (5-67) there were 11 males and 13 females.

Methods

On the day of surgery dynamic tonometry was performed before following premedication and during general anesthesia. Some of the patients got their premedication early in the morning before examination could be performed. The group of patients examined before premedication counts therefore only 11 subjects (18 eyes). In the first two cases (4 eyes) dynamic tonometry was performed before premedication and during general anesthesia. Later on it was found preferable also to include an examination following premedication which was done in the remaining 22 patients (35 eyes).

Dynamic tonometry is performed during topical anesthesia (oxibuprocaine) just like an ordinary Schiotz tonometry. The dynamic tonometer is made according to the known principles of electronic tonometers with certain important modifications (Horven 1968). In its present state the tonometer yields an output of 1 mV per 1 μ plunger deflection. An output of 50 mV therefore corresponds to a plunger movement of 50 μ which equals one scale reading Schiotz. When high sensitivity is employed the tracings may be kept on the running paper by use of a zero suppression unit thus offering the possibility to study the corneal indentation pulse amplitudes with a sufficient degree of accuracy. Normally the amplitudes are of the same order of magnitude in the two eyes and average about 30 μ of plunger movement i.e. about 0.6 scale reading Schiotz (Horven 1970 b).

Premedication In adults a slight sedative effect was obtained by use of the phenothiazine derivatives Phenergan (promethazine) 25 mg or Pacatal (mepazine) 100 mg given orally one hour prior to general anesthesia. In children a more pronounced sedation was obtained by use of Seconal (meballymal) 100-150 mg given orally one hour prior to general anesthesia. Intramuscular administration of atropine was employed in all cases.

General anesthesia In most of the cases general anesthesia was initiated by intravenous injection of Thiopentone (thiomebumal) 150-400 mg followed by Curacit (succinyl choline) 40-80 mg and in all cases endotracheal tubing. The general anesthesia was maintained by Halothane (Fluothane) N O O or in some cases by ether. In a few cases barbiturates and succinyl choline were not employed the general anesthesia being initiated and continued by ether and later on switched over to Halothane N O O.

Results

The results obtained are summarized in Table I. The eye tension was converted into mm Hg intraocular pressure by use of Friedenwald's 1955 P_0 converting table and the pulsesynchronous change in mm³ ocular volume (ΔV) was calculated from the corneal indentation pulse amplitudes by use of Langham, Het and Eriksen's data as previously described (Horven 1960a).

A marked and striking decrease in corneal pulse amplitudes and corresponding changes in ocular volume was demonstrated during general anesthesia. No difference existed between ether and Halothane in this respect. The decrease in corneal indentation pulse amplitudes was present in all but one of the cases studied. In this one case no change in amplitudes was noted whereas in another case the amplitudes were actually recorded to be zero in both eyes. Most of the cases demonstrated a marked decrease in both eyes to an average of about 33%.

Table I

Corneal indentation pulse amplitude (μ) pulsesynchronous change in ocular volume (ΔV) and intraocular pressure in mm Hg (P) recorded before premedication following premedication and during general anesthesia

		Mean	σ	%	t value
Before	μ	31.44	10.992	100	
premedication	ΔV	3.30	1.63	100	
(N = 15)	P	17.9	6.673	100	
Phenergan	μ	33.00	18.56	105	0.247
Atropine	ΔV	3.9	3.015	170	0.654
(N = 11)	P	18.66	11.794	103	0.34
Facatal	μ	6.39	1.170	84	1.311
Atropine	ΔV	0.50	0.53	16	1.613
(N = 9)	P	15.63	1.997	90	0.978
Seconal	μ	13.13	3.041	53	3.776 xxx
Atropine	ΔV	1.9	0.79	54	3.093 xx
(N = 16)	P_0	16.06	9.564	93	0.9
General anesthesia	μ	10.43	7.393	33	6.113 xxx
(N = 11)	ΔV	1.04	0.91	33	5.100 xxx
	P	13.33	6.375	77	0.093 x

Significant levels x - xx = 1% xxx = 0.1%

of the normal preanesthetic value. As judged by the Student's *t* test this decrease was significant at the 0.1% level.

A significant decrease in corneal indentation pulse amplitudes was also initiated by premedication with Seconal while Phenergan and Pacatal yielded smaller and non significant changes in the corneal pulse amplitudes.

During general anesthesia a small decrease was also noted in the intraocular pressure with a mean P_o value of 17.29 mm Hg before premedication compared with 13.38 mm Hg during general anesthesia. This will roughly correspond to eye tension levels of scale reading 5 before premedication and 6.5 during general anesthesia as measured by the 5.5 g plunger weight.

A typical recording is demonstrated in Fig. 1 which shows the change in corneal pulse amplitudes caused by Seconal. This patient was almost asleep when the recording was performed. In patients with only a slight effect following Seconal administration the corresponding decrease in corneal pulse amplitudes was less pronounced.

Fig. 2 shows the tachycardia induced by preoperative atropine and the decrease in corneal pulse amplitudes caused by ether and later on by Halothane general anesthesia. Barbiturates were not given in this case.

Fig. 3 demonstrates the effect of intravenous injection of Thiopentone on the corneal pulse amplitudes. As the patient falls asleep the amplitudes yield a corresponding significant decrease. Change in blood pressure or intraocular pressure levels may not be responsible for the decrease in corneal indentation pulse amplitudes which exists during general anesthesia, as these parameters were unchanged in this case and other cases. When a very deep anesthesia level

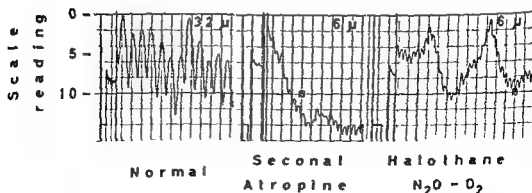
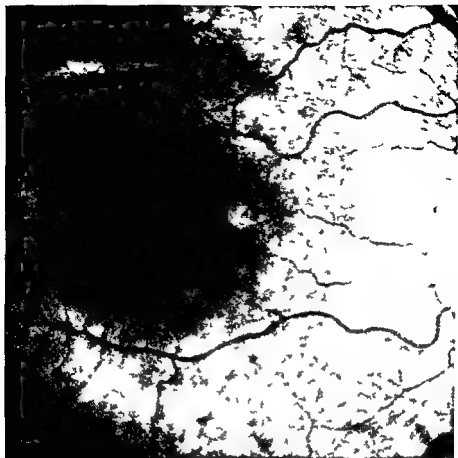


Fig. 1

Decrease in corneal indentation pulse amplitudes induced by Seconal and maintained by Halothane $N_2O - O_2$. Sensitivity settings: 20 and 2 mV per paper division.

A



B

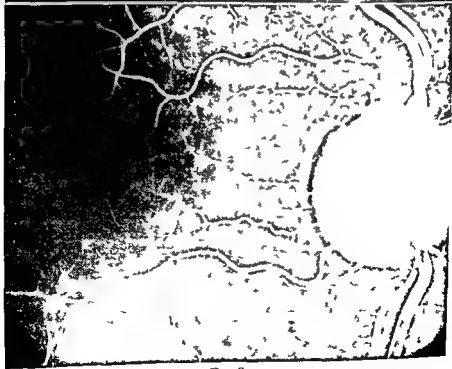


Fig 3

Case 1 14 vision 0.5 A A slight indication of a wheel like formation in the macula

B Angiogram showing intact pigment epithelium in the macula



C



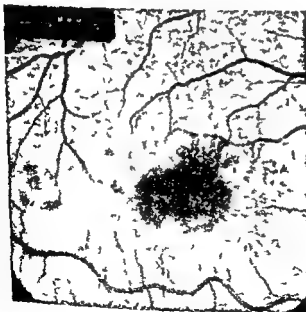
A

Fig 10

Case 8 34, vision 0 1 A Retinal vascula
veil, patches of atrophic pigment epi
thelium B Peripherally of the veil a
fluorescent vein is seen (arrow) the blood
in the main trunk is in part non fluor
escent The blood coming from the veil
is poor in fluorescent The large vessels
of the choroid are clearly visible

B





B

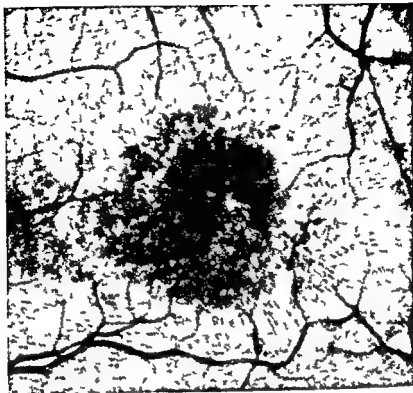
Fig 4

Case 9 20 vision 10 A A definite wheel like formation and perimacular radiate streaks B Angiogram showing normal pigment epithelium

REFERENCES

- Andrieu P: Langiographie fluorescéinique dans le décollement juvénile. *Ann Oculist* (Paris) 90: 12 1177 (1968)
- Anderson J R: Anterior dialysis of the retina. Disinsertion or avulsion at the ora serrata. *Brit. J. Ophthalmol* 16: 705 (1932)
- Bergliss B and Linder B: Sex linked hereditary juvenile retinoschisis. *Acta Ophthalmol* 45: 411 (1967)
- Bohringer H R, Duterle P und Landolt E: Zur Klinik und Pathologie der Degeneratio hyaloideoretinalis hereditaria (Wagner). *Ophthalmologica* 139: 330 (1960)
- Forsius H, Vainio-Mattila B and Eriksson A: X linked hereditary retinoschisis. *Brit J Ophthalmol* 46: 678 (1962)
- Forsius H, Eriksson A and Vainio-Mattila B: Geschlechtsgebundene erbliche Retinoschisis in zwei Familien in Finnland. *Klin. Wbl. Augenheilk.* 143: 806 (1963)
- Franceschetti A, François J et Babel J: Les hérédodégénérescences chorio rétiennes. Vol II 834 (1963) Masson et c^e. Paris
- Lenke L, Jütte A und Schenke A: Differentialdiagnose des Melanocytoblastoms der Aderhaut mit Fluorescein Natrium v. Graef. *Arch. Ophthalmol* 175: 58 (1968)
- Ley J: Inherited retinal detachment. *Brit J. Ophthalmol* 36: 626 (1952)
- Mooney H R and Alcus D L: A method of photographing fluorescence in circulating blood in the human retina. *Circulation* 24: 82 (1961)
- Sorsby A, Klein M, Gann J H and Siggens G: Unusual retinal detachment possibly sex linked. *Brit J. Ophthalmol* 35: 1 (1951)
- Thomson E: Memorandum regarding a family in which neuro retinal disease of an unusual kind occurred only in the males. *Brit J. Ophthalmol* 16: 681 (1932)
- Vainio-Mattila B, Eriksson A B and Forsius H: X chromosomal recessive retinoschisis in the region of Pori. *Acta ophthalmol* 47: 1135 (1969)
- Janoff M, Rahn E. A. and Zimmerman L. E: Histopathology of juvenile retinoschisis. *Arch Ophthalmol* 79: 43 (1968)

A



B



Fig 5

Case 3, 19, vision 0.7 *A* Moderately severe macular changes *B* Angiogram showing defects in the pigment epithelium

IMMUNHISTOLOGICAL STUDIES ON HUMAN DIABETIC AND NON DIABETIC EYES

I Fluorescent labelling of insulin and insulin antibodies

By

A U Werner and H -W Larsen

Published in *Acta Ophthalmologica*, 47 (1969) 937-955

IMMUNHISTOLOGICAL STUDIES ON HUMAN DIABETIC AND NON-DIABETIC EYES

II Autoradiography using 125 I labelled insulin, and application of histochemical procedures

By

H -W Larsen and A U Werner

Published in *Acta Ophthalmologica*, 47 (1969) 956-971

Discussion

B Rosengren (Gothenburg)

Some years ago an elderly sanatorium physician mentioned that he had never seen retinopathia diabetica in a patient with pulmonary t b. In my private practice I have endeavoured to ascertain whether there is evidence for a negative correlation between the diseases mentioned. What I have found is two patients with t b. of long standing who have had diabetes for about 35 years. In neither case could any modification of the eye ground be detected by ordinary ophthalmoscopy. Possibly the method mentioned would be capable of casting light on the question of a possible relationship.

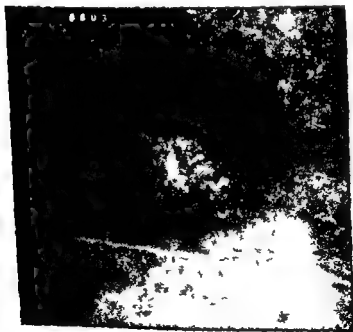


Fig 6

Case 4 44 vision finger counting 4.5m A Atypical coarsely granular destruction of the macula B Angiogram in which the choroid shows through

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INTRAOCULAR FEEDBACK MECHANISMS OF THE INTRAOCULAR PRESSURE IN RABBITS

By

Hallvard Valebjørg

Introduction

Pseudofacility' was defined by Barány (1963 1967) as the number of $\mu\text{l}/\text{min}$ by which the aqueous humor formation in the eye is reduced for every mm Hg pressure rise. This is a facility which does not help outflow. One factor in the pseudofacility is the decreased ultrafiltration rate as a consequence of the increased intraocular pressure. Barány suggested that there may perhaps be more mechanisms by which fluid production could become pressure sensitive. If they exist, they contribute to pseudofacility'.

The pseudofacility may be considered a negative feedback mechanism. By use of a new method posterior bulbus fenestration which allows a direct inspection in vivo of the vessels of the ciliary body and the choroid in the rabbit (Valebjørg 1963, 1970a), various vascular changes have been observed during artificially raised intraocular pressure. Based on these vascular responses three different feedback mechanisms have been postulated, one of which results in a reduced aqueous formation and is thus included in the pseudofacility.

A feedback mechanism may be defined as a process in which a fraction of the output is returned to the input stage (Fig. 1).

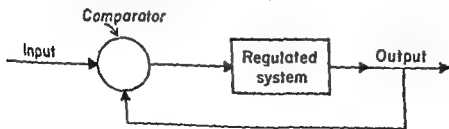


Fig. 1
The principle of feedback systems.

A simple example is provided by the servo-assisted motor. If the decrease or increase in speed of rotation is regulated in such a way that the system is brought nearer to a given speed (Sollwert) the process is called



A



B



C

Fig 7

Case 5 68, vision finger counting
3.5m A Localized macular pro
cess B Stronger fluorescence tem
porally C Large choroidal (?)
blood vessel the strongest fluor
escence ■ seen nasally

negative feedback. Positive feedback, on the other hand, would respond to an increase in speed of rotation by a further increase, and so on, yielding an unstable system.

Two important factors influence the intraocular volume and therefore the intraocular pressure:

(1) The volume of the intraocular blood vessels

(2) The volume of the aqueous humor produced across the blood aqueous barrier per unit time. This production is achieved by processes of ultrafiltration, secretion and diffusion (Kinsey and Reddy 1964).

Material and methods

The results presented are based on observations in 7 eyes of adult albino rabbits in which the ciliary epithelium is almost devoid of pigment, and the underlying blood vessels therefore can easily be studied by the method of posterior bulbus fenestration. The animals were anesthetized with a mixture of chloralose and urethane. The intraocular pressure, recorded via a cannula inserted through the cornea, and the systemic blood pressure were measured continuously throughout the experiments. Variation in intraocular pressure was effected by alteration of the height of a saline reservoir connected to a second cannula inserted into the anterior chamber through the cornea.

Results

(1) *Vascular negative feedback mechanism* — After completion of surgery the resting level of the intraocular pressure was about 15 mm Hg. Elevation of the intraocular pressure from 15 to 19–20 mm Hg caused a narrowing of the capillaries, the venules and the marginal veins of the ciliary processes (translental inspection) as well as of the choroidal veins (retrolental inspection). At higher pressure there was also a narrowing of the arterioles of the ciliary processes. The effects increased by increasing the intraocular pressure. The reduction in volume of the vascular system represents a *negative feedback mechanism*. This is included in the "Intraocular vascular system" in Fig. 2.

A few minutes after the elevation of the intraocular pressure the narrowing of the vessels was followed by a slight dilation of some venules and some of the coarser capillaries as part of a vascular recovery phase.

(2) *Vascular positive feedback mechanism* — The choroidal veins were especially sensitive to increased intraocular pressure at the point where they bend around the scleral margin just inside the trans scleral opening to emerge into the vortex vein (Fig. 3). Significant depression, or flat



Fig 8

Case 6 53 vision 0.2 Angiogram showing defects of the pigment epithelium in particular in the perimacular area

terminal stage of the macular process. With increasing age all patients are likely to exhibit similar features.

Fig 8 shows another type of pigment epithelial destruction. The macular region is less severely affected, but the angiograms reveal extensive pigment changes in the perimacular area.

Certain facts concerning the circulation in retinoschisis have been clarified with the aid of fluorescein angiography. Patient No. 7 with a visual acuity of finger counting 3 m shows the disease in severe form. The lower temporal vein is ramified (Fig 9A) with one branch running into the retinal veil and another continuing in the temporal direction. Thirteen seconds after the injection of fluorescein the temporal branch is fluorescent (Fig 9B). The blood coming from below from the veil, is not fluorescent and forms a non fluorescent streak in the main trunk. This

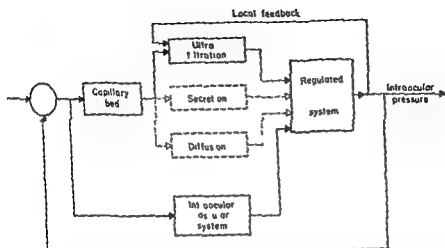


Fig 2

Intraocular feedback mechanisms The processes of ultrafiltration secretion and diffusion (across the blood aqueous barrier) represent the formation of aqueous humor. The processes of secretion and diffusion are less known and they are therefore indicated by dotted lines. For further details see text.

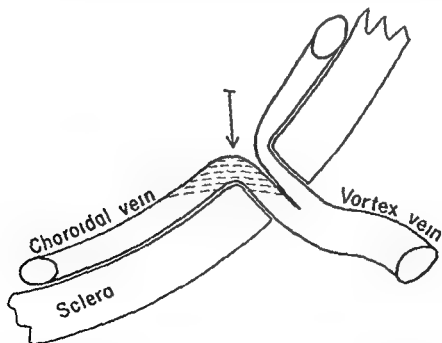


Fig 3

Schematic drawing of a vortex centre with the pressure-sensitive venous point (arrow). The dotted lines indicate the depression of the choroidal vein at the scleral opening.



A



B



C

Fig 7

Case 5 68 year old female
 3.5m A Localized macular pro-
 cess B Stronger fluorescence tem-
 porally C Large choroidal (?)
 blood vessel the strongest fluor-
 escence seen nasally

tening, of the vein on its convex side could be observed even following an increase of 1 mm Hg of the intraocular pressure. The degree of depression increased with increasing intraocular pressure until complete cessation of the blood flow at an increase of 5 mm Hg for the smallest veins and 20–50 mm Hg for larger ones. Although the total blood flow through the pressure sensitive venous points was reduced, the blood proximal to these points, i.e., in the vein through the trans scleral opening into the vortex vein, streamed faster than before. This is the first direct demonstration of "the vascular waterfall phenomenon" previously postulated in the lung by Permutt, Bromberger Barnea and Bane (1962). The reduced outflow of blood from the choroidal veins tends to increase the intraocular pressure through their increase in volume, representing a vascular positive feedback mechanism. This process is included in the "Intraocular vascular system" in Fig. 2.

The elevated venous pressure is likely reflected in the capillaries and thus secondarily influences the aqueous formation by increasing the ultrafiltration rate.

Vascular recovery change was also observed at the pressure sensitive points.

(3) *Capillary bed feedback mechanism* — A conspicuous phenomenon seen on increased intraocular pressure was the markedly reduced blood flow through the capillary bed, as judged from the slower speed of the blood corpuscles and the reduced vessel diameter. The phenomenon was present after an increase of 4–5 mm Hg. At this pressure level (19–20 mm Hg) some of the capillaries were completely empty of blood, and this vascular effect increased by increasing the intraocular pressure. This decreased area of the capillary wall permeable to fluids reduces the aqueous humor formation. The effect tends to stabilize the intraocular pressure and may be considered as a negative feedback mechanism (Fig. 2, "Capillary bed").

Comments

The intraocular vascular negative and positive feedback mechanisms influence the intraocular volume and consequently contribute to the acute change of the intraocular pressure. The increased vascular resistance at the pressure-sensitive points at the venous outflow, i.e., the waterfall phenomenon, operates concomitant with the increased vascular resistance at the inflow in the ciliary processes. It thus helps to maintain the circulation in the choroidal veins under increased intraocular pressure. This security measure is brought into play at intraocular pressure rises as low as 1 mm Hg.



A

Fig 9
 Case 7 1. vision finger count
 ing 3m *A* The temporal lower
 vein sends a branch downwards
 into the vein (arrow) *B* Non
 fluorescent blood comes from the
 vein *C* At the end of the venous
 phase the same phenomenon is
 seen as in *B*



B



C

The capillary bed feedback mechanism results in a diminished aqueous humor formation and is thus included in the pseudofacility of Barany. The reduced ultrafiltration rate due to the increased intraocular pressure (also part of the pseudofacility) is represented by the local negative feedback (Fig. 2).

It should be noted that the vascular effects in the ciliary processes by sympathetic nerve stimulation is almost identical to that seen on increased intraocular pressure.

All these intraocular feedback mechanisms except the positive one, take part in a common process by which changes in intraocular pressure are minimized.

REFERENCES

- Bárdy E H: Pseudofacility and uveo-scleral outflow routes. Some non technical difficulties in the determination of outflow facility and rate of formation of aqueous humor. Glaucoma Symp. Tutzing Castle 1966 pp 27-51 (Karger, Basel/New York 1967).
- Bárdy E H: A mathematical formulation of intraocular pressure as dependent on secretion, ultrafiltration, bulk outflow, and osmotic reabsorption of fluid. *Invest Ophthalmol* 1963 2: 584-590.
- Atney I E and Reddy D I A: Chemistry and dynamics of aqueous humor. Pp 218-319 in Prince J H (ed) *The Rabbit in Eye Research*. Thomas, Springfield, Ill. 1964.
- Permutt S, Bromberger Barnes B and Bane H V: Alveolar pressure, pulmonary venous pressure and the vascular waterfall. *Med thorac* 1962 19: 239-260.
- Fahlgjerg H: Fenestration bulbi posterior. A method for the investigation of the function of ciliary body and adjacent organs in experimental animals. A preliminary report. *Acta Ophthalmol* 1963 41: 313-316.

streak can be followed as far as the papilla. The same phenomenon also appears in the last picture (Fig 9C), after 23 sec, although the venous phase approaches its termination.

The course is similar in case 8. In Fig 10A the lower temporal main trunk is seen to continue into the veil and a narrower branch continues peripherally of the veil over the choroid, which is atrophic. In Fig 10B the vein coming from below is fluorescent, but centrally the blood stream is heterogeneous. Obviously there is non fluorescent blood coming from the veil. The nasal main trunk is conspicuous and filled with homogeneously fluorescent blood. Throughout the course of angiography the blood stream from the veil remains unchanged (Fig 10C), although the fluorescence in the other veins decreases. These observations show that the circulation in the veil is impaired. Whether the impairment is the cause or the result of progression of the pathological process remains an open question.

The last series of pictures moreover, exhibits pigment epithelial injuries both centrally and peripherally of the vascular veil. In Fig 10C the large vessels of the choroid are therefore discernible peripherally. They seem to be normal, and since the choriocapillaris shows normal fluorescence, there is no evidence of any significant involvement of this area of the choroid.

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Head *R Tornquist, MD*

EXPERIENCES WITH RETINAL CYROSURGERY

By

Ragnar Tornquist

The first trials of freezing techniques in the surgery of retinal detachment (Bietti 1934, Deutschmann 1935, Cavara 1935, Veil and Dolfuss 1939) did not lead to general acceptance of the method. The main reason was that diathermy was more convenient to use (Bietti 1968).

About five years have now elapsed since the renaissance of cryo surgery through Kelman and Cooper (1963) and Lincoff, McLean and Nano (1964) and it may be of interest to consider its value in retinal surgery. The technical problems, even with new and improved instruments, have been considerable. From experimental and clinical studies, information has been collected concerning the biological effects of cryo techniques as a basis for comparison with diathermy.

At the Eye Clinic in Örebro 800 eyes have been treated for retinal detachment and related conditions between 1 2 1961 and 30 3 1969. Cryosurgery was performed on 272 patients (290 eyes). The total number of such operations was 366.

In the majority of operations the Kelman Retinal Cryopexie instrument (Frigitronics) was used. Cooling is produced by Freon fluid which is expanded into a vacuum through a microvalve. Warming is achieved by passing warm Freon fluid through the tip of the instrument, and the process is monitored by a temperature gauge. The instrument functions well if it is used by an experienced operator. Drift disturbances from leakage at the joints, breakage of leads in the electric temperature registration and mechanical faults in the microvalve can occur and require repair by the manufacturer.

During the last year other apparatuses were used: Amoils Cryo Pencil unit (Keeler) and the Cryal apparatus (L'air Liquide). Both instruments are well suited to retinal cryosurgery and have some advantages but also some disadvantages compared to the Frigitronics instrument. The author's experiences with these instruments are rather limited at present.

The results in the cases treated by cryotherapy are shown in Table I. In the total series healing was achieved in 84 per cent. The observation

REFERENCES

- Amalric P L angiographie fluorescéinique dans le décollement juvénile Ann Oculist (Paris) 201 12 1177 (1968)
- Andersson J R Anterior dialysis of the retina Disinsertion or avulsion at the ora serrata Brit J Ophthal 16 705 (1932)
- Berglissou B and Linder B Sex linked hereditary juvenile retinoschisis Acta Ophthal 45 411 (1967)
- Buhrerger H R Dieterle P urd Landolt E Zur Klinik urd Pathologie der Degeneratio hyalocoretinalis hereditaria (Wagner) Ophthalmologica 139 330 (1960)
- Forsius H Vainio-Mattila B and Eriksson A X linked hereditary retinoschisis Brit J Ophthal 46 678 (1962)
- Forsius H Eriksson A and Vainio-Mattila B Geschlechtsgebundene erbliche Retinoschisis in zwei Familien in Finnland Klin Mbl Augenheilk 143 806 (1963)
- Fanceschetti A François J et Babel J Les hérédo-dégénérescences chorio-rétiennes. Vol II 834 (1963) Masson et c Paris
- Lemke L Jutte A und Schenke A Differentialdiagnose des Melanocytoblastoms der Aderhaut mit Fluorescein Natrium v Graef Arch Ophthal 170 58 (1968)
- Ley J Inherited retinal detachment Brit J Ophthal 36 626 (1952)
- Mooley H R and Aliu D L A method of photographing fluorescence in circulating blood in the human retina Circulation 24 82 (1961)
- Sorby A Aleu M Gann J H and Siggins G Unusual retinal detachment possibly sex linked Brit J Ophthal 30 1 (1951)
- Thomson E Memorandum regarding a family in which neuro-retinal disease of an unusual kind occurred only in the males Brit J Ophthal 16 681 (1932)
- Vainio-Mattila B Eriksson A W and Forsius H X chromosomal recessive retinoschisis in the region of Poru Acta ophthal 47 1130 (1969)
- Yanoff M Rahn E A and Zimmerman L E Histopathology of juvenile retinoschisis Arch Ophthal 79 43 (1968)

time is between 3 months and 3 years. However, assessment of the results, especially if comparisons are made, is not possible without knowledge of the composition of the material, the indications for treatment and the types of operation.

Table 1
Retinal cryosurgery in Örebro
1966-31.3.69

	Number of eyes	
	Total	Cured
A No previous retinal surgery		
Predetachment	66	64*
Retinal detachment	181	142**
	247	206
B Reoperation	43	38
	290	244
		(84 per cent)

* Additional photocoagulation in 16 eyes

** Additional photocoagulation in 9 eyes

Since 1961 the patients at the Örebro clinic have been recruited from other regions of the country to an increasing extent (Fig. 1). Since there is only one eye clinic in the county of Örebro the group of patients who come from this area can be considered as representative of the population, while those patients who are admitted to the clinic from other areas are mostly selected cases of a complicated nature.

Fig. 1. Surgery in Örebro

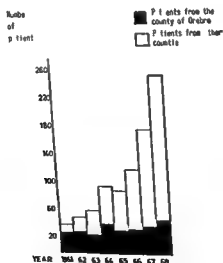


Fig. 1



Fig 9

Influence of Phenergan atropine ether and Halothane N O O on corneal indentation pulse amplitudes Sensitivity settings 90 and 2 mV per paper division

was initiated a marked decrease in both blood pressure and intraocular pressure were noted (Fig 3) The corneal indentation pulse amplitudes did however only yield a rather slight corresponding decrease

Comment

The present study demonstrates a marked and significant decrease in corneal indentation pulse amplitudes initiated either by sleep following Seconal or Thiopentone administration or by ether or Halothane general anesthesia This decrease of corneal pulse amplitudes does not seem to be caused by a change in blood pressure as the blood pressure was unchanged in many of the cases studied

During general anesthesia a minor but significant decrease of the intraocular pressure was noted To a small extent this decrease of intraocular pressure may participate in explaining the decrease in corneal indentation pulse amplitudes as a slight reduction in corneal pulse amplitudes occurs with a decrease in intraocular pressure (Horten 1960b) As judged by the previously presented data (Horten 1960b) the decrease in corneal indentation pulse amplitudes which exists between the eye tension level 30 and 15 as measured with the 50 g plunger weight should be less than 10% Accordingly the main cause of the marked decrease observed in corneal indentation pulse amplitudes following Seconal and Thiopentone administration and during general anesthesia is not properly explained by the slight reduction in intraocular pressure and should need some further discussion

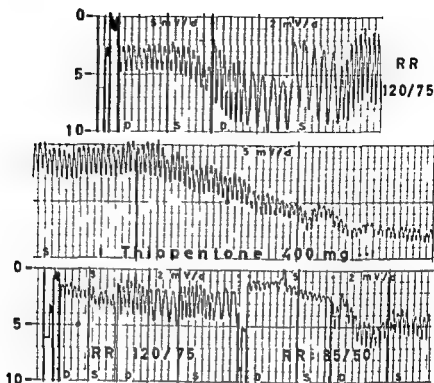


Fig 3

Influence by intravenous Thiopentone injection (middle) normal Halothane N_2O O_2 anesthesia (bottom left) and very deep Halothane N_2O O_2 anesthesia (bottom right) on blood pressure and corneal indentation pulse amplitudes. Sensitivity settings 10.5 and 2 mV per paper division.

As the corneal pulse primarily reflects the pulse-synchronous change in ocular volume initiated by the excess of blood entering the eye in systole, a decrease in corneal pulse amplitude reflects a corresponding decrease in the excess of blood which enters the eye in systole. Theoretically, this decrease may be caused either by a reduction in ocular blood supply or by a change from pulsatile to wards non-pulsatile flow or both. A strong indication that a decrease in ocular blood supply really is initiated by general anesthesia was offered by McGowan (1967) who reports a case of giant cell arteritis which turned amaurotic during general anesthesia. A similar case was recently observed in Oslo City Hospital (Bergaust 1968) in this case the diagnosis of giant cell arteritis was verified after general anesthesia was given with amaurosis as a result. Most probably these eyes which yielded no symptoms prior to general anesthesia still had a reduced ocular blood supply as a consequence of giant cell arteritis lesions in their ophthalmic arteries, a possibility which has been proved valid in other cases of

The indications for treatment have remained unchanged since 1961. To a great extent it has been the aim to operate also on cases with a poor prognosis and re operations have been performed so long as there has been any chance of improvement. In about 5 per cent of the patients admitted for assessment surgery has not been performed. Retinal cysts comprise the majority of such cases where surgery has been considered contraindicated. In a few cases the prognosis has been regarded as hopeless or contra indications of a general nature have prevented surgery.

The method for producing the adhesive chorio retinitis was changed in June 1966, when diathermy was replaced by cryotherapy. However, during a transition period diathermy was used to a certain extent, chiefly in those cases for which this method had been used previously (Table II). At about the same time treatment by trans conjunctival cryopexy was instituted for conditions which would previously have been photocoagulated (for example, retinal tears near the ora serrata).

Table 2
Methods of retinopexy Örebro 1961-1969

Year	Number of operations			Total
	Photocoagulation	Diathermy	Cryopexy	
1961	19	32		51
1962	32	41		73
1963	24	52		76
1964	36	73		109
1965	27	51		78
1966	35	59	38	132
1967	31	47	89	167
1968	36	36	191	263
1969-30 3	3	0	48	51
Total	243	391	366	1 000

The technique for producing chorio retinal contact at operation has remained constant. If a retinal elevation was present scleral buckling was usually performed with a silicone plomb according to the principle of Custodis. Evacuation of subretinal fluid was generally avoided. If this was done it was often combined with injection of air. Only in particularly complicated cases encircling procedures were performed. In some cases the silver ball method of Rosengren (modified by Klotz) and vitreous implantation were performed.

For comparison between the cryo and diathermy methods cases with manifest retinal detachment not previously operated on were selected. Prognostically unfavourable cases were collected in a group ('complic'), which included the following types of cases

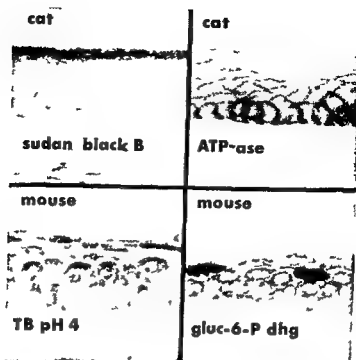


Fig. 2

Localization of lipids (sudan black B), ATPase RNA basophilia (Toluidine blue pH 4) and glucose 6 phosphate dehydrogenase in the corneal epithelium

Table 2

Effect of some ions and pharma on the activity of acid phosphates and ATPase in the corneal epithelium

	Acid phosphatase monkey rabbit (mM/l)	ATPase monkey (mM/l)
Mn ⁺⁺	activates (10 0)	activates (10 0)
Mg ⁺⁺	activates (10 0)	activates (6 0 54 0)
Cu ⁺⁺	inhibits§ (1 0 10 0)	inhibits* (5 0 10 0)
F ⁻	inhibits§ (10 0)	inhibits* (10 0)
■ atrophantin	no effect§ (0 1 1 0)	no effect* (0 1 1 0)
acetazolamide	no effect§ (1 0)	no effect* (0 5)
atropine sulphate	no effect§ (1 0)	no effect* (10 0)
pilocarpine chloride	no effect§ (1 0)	no effect* (10 0)
cocaine chloride	no effect§ (1 0)	no effect* (10 0)
physostigmine salicylate	no effect§ (1 0)	no effect* (5 0)

Any effect estimated by comparing sections incubated with and without the substance examined

§ Mn⁺⁺ (10 0 mM/l) added as activator

* Mg⁺⁺ (10 0 mM/l) added as activator

- 1 No tears visible
- 2 Constant tears, multiple holes in more than one quadrant
- 3 Total detachment
- 4 Preretinal traction
- 5 Examination difficult (non cooperative patient, cloudy media posterior synechia etc)

The remaining cases composed a more homogenous group (simple) with a better prognosis. The comparison between the diathermy and cryo methods in the two groups is shown in Table III. The differences between the two methods are not significant.

Table 3
Cases of retinal detachment with no previous retinal surgery

Method	Retinal detachment	Number of eyes	
		Total	Cured
Diathermy	simple	100	89 (89%)
	complic	161	109 (68%)
	total	261	198 (76%)
Cryopexy	simple	103	95 (92.5%)
	complic	78	47 (60.3%)
	total	181	142 (78.5%)

The frequency of complications with cryotherapy is probably low. Insufficient choro retinal adhesion is not to be feared according to experimental studies. Assessment of the effect is made at operation, either with each application (treatment of small areas well seen ophthalmoscopically) or after single test application whereat temperature and time are noted. Freezing is stopped when the choroid becomes grey white that is when the choroidal temperature falls below freezing point. If retina is brought into contact with the wall of the globe by pressure with the instrument a white discoloration of the retina is seen more clearly. Clinical experience shows that in spite of this control poor adherence is sometimes obtained postoperatively. This happened in 14 cases and re-operation was necessary. Experience shows that especially with choroidal atrophy one should apply more powerful freezing or combine the procedure with photocoagulation.

Retinal and choroidal haemorrhage can occur with cryotherapy if when the instrument is frozen onto the sclera it is removed quickly without defreezing. Damage to tissues is then produced and usually small capillary haemorrhages result. With proper care however this risk is probably small. The walls of the larger vessels are not damaged by

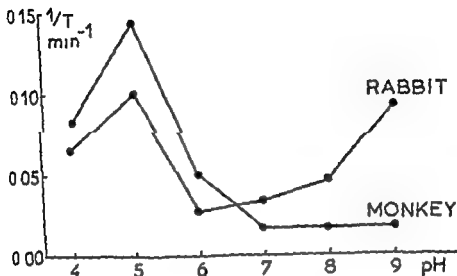


Fig 3

pH dependence of phosphatase activity in the superficial cells of the corneal epithelium. The reaction intensity is given as the reciprocal of the time in minutes to positive reaction

while in cat and pig only the basally localized activity was found. The alkaline phosphatase reaction took place at pH 8-10. It was markedly weaker at pH 7 and had disappeared at pH 6. In animals showing acid as well as alkaline phosphatase superficially in the epithelium two reaction maxima could be observed (Fig. 3) showing the presence of two different enzymes.

In all the species investigated glycogen and the enzymes from the oxidative metabolism could be demonstrated (5). Enzymes from the pentose shunt, especially glucose 6-phosphate dehydrogenase (NADP) varied in intensity from one cell to the next. Cells with high activity (Fig. 2) also showed a high content of RNA. This suggests a protein synthesis but the particular function of these cells is unknown. Mitoses are only rarely seen above the basal layer and the cells do not differ morphologically from the surrounding cells.

The cells appearing morphologically different in sections have never been observed to differ metabolically from the surrounding cells.

Physiological studies

Enzymatic differences are present among animal species even among the frequently used experimental animals as rabbit, rat, cat and monkey. Also in other respects there seem to be functional differences. An electrical

freezing and no haemorrhage from these has been observed. However, a hyperaemia of the treated areas develops some minutes after treatment. This may be the reason for the accidental haemorrhage in association with puncture through a previously frozen area (Bietti 1968). In our material intra- and sub-retinal haemorrhage has occurred in 8 cases in association with the release of subretinal fluid after cryotherapy. It is advisable to refrain from this procedure, and if possible the puncture should be performed within areas which have not been frozen.

The advantages of cryotherapy thus do not comprise better and more certain healing between the retina and the wall of the globe. Indeed, in some cases the adherence is weaker. But the risks of serious complications are probably less than with diathermy. Those relatively common completing operations which are probably unavoidable in retinal surgery (because of poor retino-choroidal contact, weak adherence, etc.) are made considerably simpler because re-operation is easier to perform and not usually associated with greater risks than the primary operation. The intact scleral wall also makes erosion of the sclera with encircling suture according to Arruga less likely. In only one case out of 44 when cryotherapy was applied with an encircling procedure has a small erosion been seen.

At the Örebro clinic we feel that at the moment we are able to dispense with the diathermy operation for retinal surgery cases. The importance of good postoperative chorio-retinal contact is probably greater than with the diathermy operation and the surveillance of the development of the chorio-retinal adherence around the retinal hole must be more careful. Probably it is necessary to complement the operation with photocoagulation to a greater extent. The essential advantage is more lenient treatment of the eye. It seems to be a progress in the development of retinal surgery with its trend towards more complicated and traumatic operations.

REFERENCES

- Bietti G B. *Acta XIV Conc. ophthalm. (Madrid)* Vol 2 p 12 1933
 Bietti, G B. *Klin Monatsbl Augenheilk.* 157 181 1968
 Casara, V. *Boll ocul.* 14 1307 1935
 Deutschmann R. *Klin Monatsbl Augenheilk.* 104 349 1935
 Kelman C D and Cooper I S. *Eye Ear Nose and Throat Month.* 42 42 1963
 Lincoff H A, McLean J and Lano H. *Trans Amer Acad Ophth Otolaryngol.* 68 412 1964
 Tornquist, R. *Acta Ophth.* 46 529 1968
 Veit, P and Dolfuss M. *Traktat ophth.* 7 745 1939

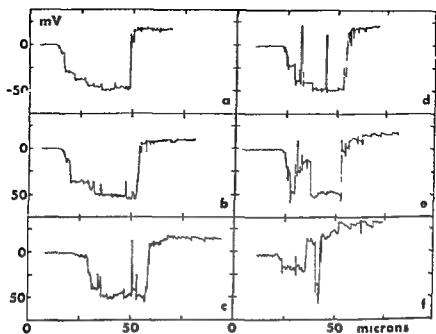


Fig 4

Typical potential recordings from penetrations of rabbit corneas. Abscissa: position of microelectrode. Ordinate: potential in mV. The time of penetration is about 30 sec. The electrode is moved from left to right. In a, b and c the transcorneal hydrostatic pressure was 18 mm Hg; in d 29 mm Hg; and in e and f 37 mm Hg. In experiments e and f the endothelium was scraped off.

potential difference of 15–20 mV exists across the rabbit corneal epithelium, with the outside negative in relation to the stroma (4). This potential difference has been demonstrated in the ox, but not in man or cat.

Intracellular potentials. The electrical potential profile through the epithelium was studied by means of microelectrodes with a tip diameter of 0.25μ (6). Negative intracellular potentials of about 40–50 mV were recorded in all experiments on rabbit, cat, ox, rat, and dog corneas. Only rabbit and cat were subjected to closer studies (Figs 4 & 5). The fall in potential in the surface of the epithelium often occurred over a distance of 5–10 μ , after which no regular changes were seen until a sudden change in positive direction occurred at the basement membrane. In the rabbit an overall transepithelial potential of about 15 mV with inside positive was found (Fig 4). In the cat no transepithelial potential could be demonstrated.

In about 50 per cent of all penetrations positively directed peaks were recorded within the epithelium. The peaks reached the level of the inside potential, but this was never exceeded. The number and the width of the peaks increased when the transcorneal hydrostatic pressure was increased.

Discussion

B. Rosengren (Gothenburg)

In the nineteenth century one tabulated three conditions which had to be fulfilled if one was to expect healing of a detached retina according to a principle of Conin.

1 The operation had to be performed at the site of the rupture or ruptures. The question of identification was therefore very important. By practise an ophthalmoscopic examination could reveal about 95 % of the retinal holes. The reason for an unsuccessful outcome could therefore rarely be blamed on a failure to identify the ruptures.

2 Coagulation had to be performed around the rupture. By the introduction of diathermy in 1930 this condition was easily fulfilled.

3 A physical contact between the retina and the choroid had to be achieved by some means in order to expect healing. This was a very difficult problem. Before the introduction of methods which had a clear and sound theoretical basis the success rates were below 50 %. In my own case the outcome of operations on 29 patients in the years 1933-36 resulted in a success rate of 45%.

In 1936 I started to examine the operated eyes (with an ophthalmoscope) only a few days after the operation and in some cases I noticed that the detachment was very high. I tried to inject air into the vitreous body in order to produce a pressure which could approximate the retina to the choroid in the region of the rupture. This procedure resulted in an immediate increase of the success rate to 78% and this figure was more or less constant from 1936-1954. During these years this method was used as routine at eye-clinic in Göteborg.

The buckling operations which were introduced by Landener in 1933 had in the beginning a very uncertain theoretical basis and the results of the operations were very difficult to evaluate. The rationale behind the operation was to decrease the size of the sclera to accommodate the detached retina. The method was improved by Shapland who in 1951 produced a buckle by lamellar resection of the sclera. In 1949 Custodis demonstrated a spontaneous regression of the detachment by placing the buckle exactly adjacent to the rupture. This important observation has made this method the one of choice to obtain contact between the detached layers during the healing period. By using this procedure the usual success rate is in the order of 80-85%. If the contact operations were to be given up one would expect to return to the old success rate figures of less than 50%.

The question in our context is however what influence the new cryotherapy will have on the success rate. It is evident that this method is less destructive than ordinary electrodiathermy. One will therefore expect less retinal damage in the central areas and a better visual acuity in the successful cases. In addition it causes very little scleral damage and this makes a reoperation easier.

Is the electrodiathermy coagulation not realistic therapeutical alternative nowadays? The question cannot be answered at present. If an improvement in the diathermy method could produce as undestructive and uniform lesions as seen by the cryotherapy method it would through its simple construction offer an alternative.

Finally I would like to congratulate Docent Tornquist with his very high success rates. The thorough and very critical evaluation of the cases give these figures an additional value.

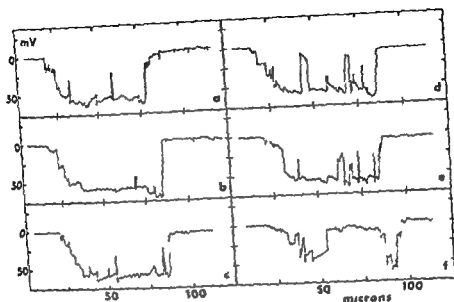


Fig 5

A sequence of penetrations from a cat cornea. a, b and c are recordings at 15 min intervals. Transcorneal hydrostatic pressure 20 mm Hg. In d, e and f the transepithelial hydrostatic pressure was 45 mm Hg. The pressure had been maintained for 30 min before the recordings were made at 15 min intervals.

This procedure is known to dilate the intercellular spaces, and it is probable that the peaks represent intercellular spaces in direct communication with the inside.

Comments

The corneal epithelium is very regular, showing only small morphological species variations. In the surface cells lipids may be demonstrated probably originating from the Meibomian glands and taken up by the cells by pinocytosis.

Cells of different morphology are seen in the epithelium, but demonstration of enzymatic differences between morphologically different cells has proved unsuccessful. Tissue culture studies did not show several types of cells. As the morphological differences could always be explained stereometrically when the orientation of the sections was carefully considered, it must be concluded that proofs of the existence of several functionally different cell systems in the epithelium have been given neither in literature nor in the present studies.

The transepithelial potential demonstrated in the rabbit is a function of the entire epithelial layer, whereas the energy requiring processes probably occur as ion transports across the surface membrane of the

freezing and no haemorrhage from these has been observed. However, a hyperaemia of the treated areas develops some minutes after treatment. This may be the reason for the accidental haemorrhage in association with puncture through a previously frozen area (Bietti 1968). In our material intra- and sub retinal haemorrhage has occurred in 3 cases in association with the release of subretinal fluid after cryotherapy. It is advisable to refrain from this procedure, and if possible the puncture should be performed within areas which have not been frozen.

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REFERENCES

- Bietti, G. B. *Acta XIV Conc. ophthalm. (Madrid)* Vol 2 p 12 1933
 Bietti, G. B. *Klin. Monatsbl. Augenheilk.* 152 181 1968
 Cataro, V. *Boll. ocul.* 14 1307 1935
 Deutschmann, R. *Klin. Monatsbl. Augenheilk.* 104 349 1935
 Kelman, C. D. and Cooper, I. S. *Eye Ear Nose and Throat Month.* 49 42 1963
 Lincoff, H. A., McLean, J. and Vano, H. *Trans. Amer. Acad. Ophth. Otolaryngol.* 68 412, 1964
 Tornquist, R. *Acta Ophth.* 46 529 1968
 Veit, P. and Dolfuss, M. A. *Traité opht.* 7 745 1939

individual cells. The "box profile" of the intra epithelial potentials with approximately the same negative level in all cells suggest that these are electrical in parallel. It is still unknown how the functions of the cells are integrated. The ionic composition of the bathing fluids influence the potentials. The surface potential is sensitive to sodium and anions, the potential change at the basement membrane is potassium sensitive. Species differences in the composition of the tears and the interfibrillar fluid of the stroma may explain why no transepithelial potentials have been demonstrated in the cat and the human cornea (4,6). Another explanation is that no potential difference is maintained *in vivo*. It is, however, difficult to demonstrate the lack of a potential.

If there are species differences in the existence of a transepithelial potential, it is tempting to correlate these with species differences in enzyme content. In this respect the superficially localized alkaline phosphatase is interesting. In the rabbit and the ox both transepithelial potential and phosphatase activity are found, in man and cat both are lacking. Further studies on this possible correlation are needed. It must be concluded that whereas negative intracellular potentials appear to be a general biological phenomenon, it is still unknown if a transepithelial potential is of more general occurrence and should be considered in the maintenance of the normal functions of the cornea.

REFERENCES

1. Bulow N and Ehlers N (1968) Morphology and DOPA reaction of cultivated corneal epithelial cells. *Acta ophthal* 46: 749-756.
2. Ehlers N (1965) The precorneal film. Biomicroscopical, histological and chemical investigations. *Acta ophthal suppl* 81.
3. Ehlers N (1965) Corneal adenosine triphosphatase. An histochemical investigation. *Exp Eye Res* 4: 48-53.
4. Ehlers N and Ehlers D (1968) Effects of hydrostatic and colloid-osmotic pressure on electrical potential and short circuit current across the explanted rabbit cornea. *Acta ophthal* 46: 767-778.
5. Ehlers N (1970) Morphology and histochemistry of the corneal epithelium of mammals. *Acta anat* 75: 161-198.
6. Ehlers N (1970) Intracellular potentials of the corneal epithelium. *Acta physiol scand* 78: 471-477.

SOME COMPARATIVE STUDIES ON THE MAMMALIAN CORNEAL EPITHELIUM

By

Niels Ehlers

The corneal epithelium has been the object of many investigations but in spite of this, problems of structural as well as functional nature remain. Some of these however are only apparent originating in the use of different techniques and of different animal species. This paper presents the results of some comparative studies, parts of which have been reported elsewhere (see references).

Histological studies

Table I shows the mammals included in the studies. The thickness of the epithelium and the number of cell layers vary from one species to the next. The epithelium is generally thinnest in the centre of the cornea, and thickness and number of cell layers increase towards the limbus. Compared with the difference in size of several of the species investigated the thickness and the number of cell layers show little variation.

Morphology The cells of the epithelium are described as being in three layers: a basal, an intermediary and a superficial layer. The size of the superficial and intermediary layers varies. In the ox the intermediary layer is the largest. In whale and seal an extremely highly developed superficial layer with well over ten layers of flattened cells is found, while the intermediary layer comprises only a few layers of cells. The many superficial cells are probably a protection against the hypertonic sea water.

In all species examined the epithelium is stratified squamous and non-keratinized. In older literature it is mentioned that the epithelium is keratinized in the whale. During the present investigations (5) it has not proved possible to demonstrate keratohyalin granules in the epithelium of the whale nor have the special stainings (mercury orange) given support to the supposition of keratin formation.

In the literature descriptions of various kinds of cells in the epithelium are found. Apparently each author has observed a new kind of cells. It is

ACTA OPHTHALMOLOGICA Vol 48 1970

CHANGES IN THE MOLECULAR MORPHOLOGY OF
THE VITREOUS AFTER INTRAOCULAR SURGERY

By

Sven Österlin

The hyaluronic acid concentration in the vitreous of aphakic eyes is considerably lower than in the corresponding phakic eyes. The implications of this finding in relation to the importance of the hyaluronic acid in the molecular morphology of the vitreous and to the post operative changes in the vitreous following uneventful intracapsular lens extraction is discussed.

To be published in final form in the Transactions of the XIX World Congress of Ophthalmology

ACTA OPHTHALMOLOGICA VOL 48 1970

DEAD, DEGENERATE, AND LIVING CELLS IN
CONJUNCTIVAL FLUID AND MUCOUS THREAD

By

M S Norn

Published in *Acta Ophthalmologica* 47, (1969), 1102-1115

ON TRANSPLANTATION OF CORNEA AND PERILIMBAL SCLERA IN RABBITS

By

J. Hetland-Eriksen

To be published in *Acta Ophthalmologica*

Discussion

H. Valebjørg (Oslo)

This is the age of transplantations, and I would like to mention a case where acrylic has been used. This plastic causes very little tissue irritation. The first illustration shows the acrylic window placed in the sclera just behind the ciliary body (Valebjørg, 1963). As result of the operation some blood corpuscles appeared just behind the lens, and these corpuscles were later organized. The conjunctiva from the palpebra and the bulbus encircled the fenestration and resulted in complete apposition to the window. The eye was pale and free from reactions. One could demonstrate a normal pupillary reaction and I had the impression that the rabbit had a normal vision on this eye. A year after the operation an acute inflammation of the bulbus appeared (injury?). The intraocular condition, however, showed no changes.

The illustration demonstrates the fenestration of the bulbus.

Ref. Valebjørg H. Fenestration bulbi posterior. A method for the investigation of the function of ciliary body and adjacent organs in experimental animals.

A preliminary report. *Acta Ophthal* 1963 41, 313-316.



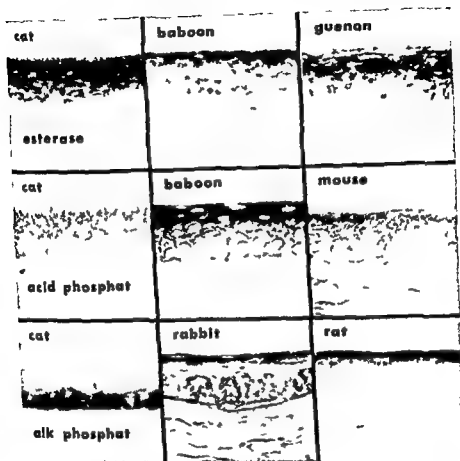


Fig 1

Histochemical enzyme reactions in the corneal epithelium. Naphthol As-acetate esterase and acid naphthol AsBi phosphatase is localized mainly to the superficial cells. Alkaline naphthol AsBi phosphatase shows species variations in localization.

preted as pinocytosis of lipids originating from the Meibomian glands (2). ATPase was found to be localized in the cell membranes with the exception of those lining the basement membrane (5) (Fig 2). This enzyme is often correlated to active membrane transport. The general occurrence of acid phosphatase and of ATPase gave rise to an examination of the effect of certain ions and drugs upon the enzyme activity. The results are shown in Table II.

Alkaline phosphatase showed variations between the individual species (3,5) (Fig 1). In man and monkey no reaction occurred. In ox, dog, rabbit, guinea pig, rat and mouse a superficial reaction was found. In dog and rabbit, besides the superficial localization, a basal activity was found.

GENERAL MEETING

Gron Bahr Report on N O L R

The accounts were submitted The activities will continue as hitherto

Helger Ehlers

Report on Acta Ophthalmologica

Since my last report in Copenhagen 1967 the Acta has shown a steady progress

Volume 45 1967 and volume 46, 1968 comprised 884 and 1277 printed pages respectively During these two years nine supplementa were issued

It should be noted that the Acta from volume 47, 1969 has been printed on coated paper more fit for reproduction of fine details

The subscription rate is 120 Dkr It is felt that Acta Ophthalmologica is still an inexpensive periodical considering quality, quantity and not forgetting the supplementa which in most cases are Scandinavian doctorate theses

About one third of the whole issue is distributed in Scandinavia two thirds all over the world

Election of new Editor in Chief of Acta Ophthalmologica

Professor Holger Ehlers retires as Chief Editor of Acta Ophthalmologica at the end of 1969

Professor Poul Brendstrup was elected as new Editor in Chief from January 1970

Table I
Thickness and number of cell layers of the corneal epithelium

Animal species	Number of eyes	Epithelial thickness	Number of cell layers
man	II	30-40	5-7
baboon	6	35-45	5-7
guenon	14	30-40	5-7
vervet monkey	4	35-45	5-7
pig	9	50-70	6-9
cat	8	35-50	6-8
ox	6	90-120	10-15
dog	7	60-80	8-10
rabbit	9	30-40	5-7
guinea pig	14	30-40	5-7
rat	16	25-35	4-6
mouse	III	20-30	3-5
seal	4	60-90	10-15
blue whale	3	100-130	12-18
sperm whale	1	80-120	12-16
porpoise	4	40-60	10-14

The thickness in μ and the number of cell layers refer to the central cornea. The thickness was measured on formalin or formal calcium fixed sections cut perpendicular to the surface. This fixation gives only a minor shrinkage as compared with fresh frozen sections which were unfortunately not available for all species studied.

remarkable that there exists a large number of electron microscopic examinations of the corneal epithelium which fail to mention the presence of several kinds of cells. In the present investigations (5), the existence of morphologically different cells have been verified. This, however, cannot in itself be considered proof of the existence of several kinds of cells, perhaps functionally different as the morphology observed may be explained purely stereometrically and may very well represent the differentiation of the normal cell.

During investigations of epithelial cells in tissue culture (1) with special reference to the presence of several kinds of cells in the epithelium, continuous photographing unveiled transformations between the various morphological types, and it was assumed that they represent states of the life cycle of the cells.

Cytochemistry In all the species investigated a strong, mainly superficially localized reaction for naphthol As esterase and acid phosphatase (naphthol AsBi phosphate) was found (2, 5) (Fig. 1). These two enzymes may be correlated to the occurrence of lipids in the surface of the epithelium of all species examined (Fig. 2). The function of these enzymes has been inter-



Presentation of the K K K Lundsgaard Medal

Professor Holger Ehlers presented the K K K Lundsgaard Medal in gold to professor *Arvo Oksala*, Turku, Finland, for his outstanding and progressive work in ultrasonography in ophthalmology. His activities cover methods, fundamental aspects and clinical application. Scandinavian ophthalmology and the *Acta Ophthalmologica* profited greatly from professor Oksala's steady and continued studies.

Dr Kristjan Steinsson invited to the next Nordic Meeting of Ophthalmologists in Iceland in 1971.

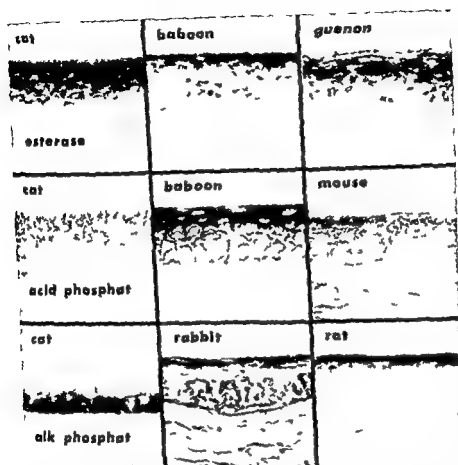


Fig 1

Histochemical enzyme reactions in the corneal epithelium. Naphthol As acetate esterase and acid naphthol AsB₁ phosphatase is localized mainly to the superficial cells. Alkaline naphthol AsB₁ phatase shows species variations in localization.

puted as a pinocytosis of lipids originating from the Meibomian glands (2). ATPase was found to be localized in the cell membranes with the exception of those facing the basement membrane (3) (Fig 2). This enzyme is often correlated to active membrane transport. The general occurrence of acid phosphatase and of ATPase gave rise to an examination of the effect of certain ions and drugs upon the enzyme activity. The results are shown in Table II.

Alkaline phosphatase showed variations between the individual species (3, 5) (Fig 1). In man and monkey no reaction occurred. In ox, dog, rabbit, guinea pig, rat, and mouse a superficial reaction was found. In dog and rabbit, besides the superficial localization a basal activity was found,

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Steinsson, Kristjan, Reykjavik

this disease (Horten 1970 c) The reduced blood supply yielded presumably sufficient nourishment of the eyes until general anesthesia initiated a further decrease in ocular blood supply with amaurosis as a result. As a consequence of this interpretation it is advisable for patients suffering from giant cell arteritis to have a dynamic tonometry examination performed prior to accepting surgery under general anesthesia. If this test demonstrates a decrease in corneal pulse amplitudes in eyes with useful vision the general anesthesia should if possible be avoided.

The present demonstration of a decrease in corneal pulse amplitudes initiated by sleep following Seconal or Thiopentone administration may also have a bearing in explaining the point stressed by Meadows (1968) that clinically the blindness in giant cell arteritis very often is noted in the morning following a good nights sleep.

As mentioned above the excess of blood entering the eye in systole will initiate a change in intraocular pressure which in man and animals may be recorded by various tonometry methods of which dynamic tonometry is preferred by the authors and in animals by a direct approach by application of a pressure transducer to a cannulated eye. Lawrence & Schlegel (1966) demonstrated in Urethane anesthetized rabbits a pulsesynchronous change in intraocular pressure of 0.2 mm Hg (normotensive eyes) and 1.5-2.3 mm Hg (hypertensive eyes). Similar results were presented in Nembutal anesthetized rabbits by Bynke (1965). The previously mentioned preliminary experiment in Nembutal anesthetized rabbits performed by one of us (I.H.) yielded results confirmative with these observations. Thus the pulsesynchronous change in mm Hg intraocular pressure reported from anesthetized rabbits is only 15-30% of the values obtained in non anesthetized human beings (Horten 1970 b). The values reported in rabbits are of the same order of magnitude however as the values obtained in man during general anesthesia. Results concerning the pulsesynchronous change in intraocular pressure and volume obtained in rabbits during general anesthesia should therefore be accepted with a large part of skepticism. As in man such results will probably not reflect the normal state of non anesthetized animals.

Summary

The corneal indentation pulse was studied before following premedication and during general anesthesia in 24 patients (39 eyes). A significant decrease in intraocular pulsation was demonstrated following Seconal or Thiopentone administration and during ether or Halothane general anesthesia.

The decrease in corneal pulse amplitudes observed during general anesthesia

most probably reflects a corresponding decrease in ocular blood supply. Accordingly, if an emergency situation does not exist general anesthesia should not be accepted by patients suffering from giant cell arteritis unless a dynamic tonometry procedure have proved their ocular blood supply to be within normal levels

Acknowledgment

The skilful technical assistance of Mrs Gull Britt Huseby is gratefully acknowledged

References

- Bergaust B. Personal communication 1968
- Bynke H G. Influence of intraocular pressure on the amplitude of the corneal pulse. A study on man and rabbits. *Acta Ophthal (Kbh)* 46: 1135-1145, 1968
- Harven I. Dynamic tonometry I. The dynamic tonometer. *Acta Ophthal (Kbh)* 46: 1213-1221, 1968
- Harven I. Dynamic tonometry II. Methods of corneal indentation pulse registration. *Acta Ophthal (Kbh)* 48: 23-38, 1970a
- Harven I. Dynamic tonometry III. The corneal indentation pulse in normal and glaucomatous eyes. *Acta Ophthal (Kbh)* 48: 39-58, 1970b
- Harven I. Dynamic tonometry IV. The corneal indentation pulse in giant cell arteritis. *Acta Ophthal (Kbh)* 48: in press, 1970c
- Lawrence C & Schlegel W A. Ophthalmic pulse studies I. Influence of intraocular pressure. *Invest Ophthal* 5: 515-525, 1966
- McGowan B L. Active temporal arteritis as a contraindication to elective surgery with general anesthesia. *Amer J Ophthal* 64: 455-457, 1967
- Meadows S P. Temporal or giant cell arteritis - ophthalmic aspects. Chapter 10 pp 149-157, in L Lawton Smith. *Neuro ophthalmology* Vol IV. C V Mosby Co. Saint Louis, 1968



Presentation of the K K K Lundsgaard Medal

Professor Holger Ehlers presented the K K K Lundsgaard Medal in gold to professor *Arvo Oksala*, Turku, Finland, for his outstanding and progressive work in ultrasonography in ophthalmology. His activities cover methods, fundamental aspects and clinical application. Scandinavian ophthalmology and the *Acta Ophthalmologica* profited greatly from professor Oksala's steady and continued studies.

Dr Kristjan Steinsson invited to the next *Nordic Meeting of Ophthalmologists* in Iceland in 1971.

Table 3
Age and sex distribution of 1882 patients subjected
to routine tonometry

age	females	males	Total
35-44	127	250	377
45-54	217	365	582
55-64	134	272	406
65-74	97	212	309
75-84	91	97	188
≥ 85	9	11	20
Total	675	1207	1882

Patients with Applanation Values Below the Screening Level

In 1713 of the 1882 patients the applanation value found was below the screening level of 20 mm Hg in both eyes

As stated previously the applanation measurement formed part of a general eye examination. This involved that in two patients glaucoma was suspected in spite of an applanation value below the screening level. One of these patients was a man aged 75 whose optic discs were characterized as glaucoma suspicious but the suspicion could not be maintained after further examinations.

In the case of the other patient – a woman aged 71 – anamnestic data were available which might be interpreted as rainbow rings around the light. Gonioscopy revealed a narrow chamber angle whereas the results of the further examinations added no support to a diagnosis of glaucoma.

According to the procedure chosen further examinations should also be offered to patients with a screening tension under 20 mm Hg if a difference of 4 mm Hg or more between the two eyes was recorded. This was so in a total of eight patients (two males and six females) ranging in age from 42 to 85.

However with a single exception the difference in tension could not be reproduced on control measurements. The optic discs were normal and the visual field tests gave normal results in the six patients whose co operation was sufficient to permit satisfactory testing.

In agreement with Davanger (1965) and Hollows & Graham (1966) the results of the present investigations thus suggest that recording of fairly great differences in tension between the two eyes in patients whose intra ocular

Holst Berg Tormod Oslo
 Horven Ivar Oslo
 Haarr Marius, Ålesund
 Ihler Jon O Skien
 Jensen Per Stavanger
 Johansen, Otto Oslo
 Klouman Otto Fredrik Kristian
 sand S
 Kolstad Albert Oslo
 Kristiansen Odd Juhus Kongs
 vinger
 Lager, Reidar, Tromsø
 Larsen Jon Bergen
 Lochte, Ragnar, Tonsberg
 Malling Birger Oslo
 Midtbo Arne Drammen
 Moi Ivar Sandefjord
 Maartmann Moe, Erik, Honefoss
 Nicolaisen, Bjorn Oslo
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 Nyquist Bengt, Bergen
 Odd Olaf Arendal
 Odland Magnus Bergen
 Omvik Per Bergen
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 Schjelderup Mathiesen Per Oslo
 Sellevold Ole Jakob Arendal
 Sokol Alf Bergen

Standal, Brynjulv Molde
 Sunde, Olav Aga, Oslo
 Syrdalen, Per, Oslo
 Thomassen, Thore Lie, Oslo
 Tjåland Johan Oslo
 Torlei Knut, Bergen
 Tveiten, Berge, Bergen
 Tønnum, Knut Tonsberg
 Uchermann, Albert Bergen
 Udyus, Ludvig Bærum
 Udnæs Ingar Oslo
 Valebjørg Hallvard Oslo
 Vallersnes Odd Haugesund
 Wursching Johan Chr Oslo
 Wursching, Ludvig sen, Kristian
 sand S
 Wursching Ludvig jr Kristian-
 sand S
 Waalen, Torbjørn Gjøvik
 Waaler, Paul Lillehammer
 Yteborg Jan Bekkestua
 Aasvold Henry, Bergen

Other countries

Gundersen Trygve Boston USA
 Holm Knut U Brooklyn, New
 York, USA
 Johnson Albin Raleigh N Caro-
 lina USA
 Jorgensen, Donald R St Paul
 USA
 Siemenstad L O Osceola Wis-
 consin USA
 Worst Jan Gerben Frans Gro-
 ningen, Holland

to an ophthalmic practice where as stated previously females have been found to attend in greater numbers than males

Further Examinations

Endeavours were thereafter made to either establish the diagnosis or refute the suspicion of glaucoma on the basis of the following lines laid down for diagnostic control examinations of the 169 screening positive cases

Control pressure measurements were arranged in ophthalmic practice within 1-3 months

Further examinations were thereafter carried through as follows in the Department of Ophthalmology *Centralsjukhuset* Nykøbing Falster

To these examinations were subjected patients with a screening pressure of 21 mm Hg or of at least one eye during 3 or 4 days stay in hospital where they had a chance of renewed determinations of vision and refraction and of ophthalmoscopy In addition they were subjected to 24 hour pressure measurements (not less than four measurements between 7 a.m. and 8 p.m.) scleral rigidity determination visual field measurement water provocative test priscol provocative test gonioscopy mydriasis test dark room test and retinal photography

Patients with a screening pressure of 20-21 mm Hg were subjected to out patient examination comprising determinations of vision and refraction ophthalmoscopy visual field measurement gonioscopy water provocative test and pressure measurement preferably between 8 and 10 a.m.

However not all the 169 patients could have the diagnostic control examinations carried through on the desired lines

Of the 169 patients 50 (29.6 per cent) failed to appear for the appointed control pressure measurements in ophthalmic practice and another eight had been admitted to hospital or been subjected to treatment immediately after the screening

Of the 89 patients with a screening pressure of 22 mm Hg or higher (see Table 4) no more than 55 had examination carried through during stay in hospital As regards the 34 patients not admitted to hospital the main reasons for this were in some cases difficulty of making them consent to admission these patients having an unaffected vision and only slight eye troubles (21 patients) while in others admission was desisted from owing to a poor general condition high age or inadequate co-operation (13 patients)

In addition to the above 35 patients another seven with screening pressures below 2 mm Hg were admitted Thus 62 patients were examined during stay in hospital

Of the remaining 104 patients, 84 had out patient examination carried through in the ophthalmic unit while 20 did not attain to this stage Seven

Sweden

Algvere, Peep, Stockholm
Anjou, Ingvar, Jonköping
Anseth, Arvid, Lund
Aurell, Elisabeth, Goteborg
von Bahr, Gunnar, Uppsala
Bergquist, Birgitta, Eskilstuna
Blix, Karin, Norrköping
Blix, Magnus, Norrköping
Bostrom-Smith, Inga-Lisa, Gävle
Bynke, Hans, Lund
Carlberg, Olof, Gävle
Dahlberg-Parrow, Ragna, Uppsala
Elg, Gosta, Kalmar
Enoksson, Paul, Stockholm
Ericson, Lennart, Uddevalla
Eriksson, Anna Stina, Boden
Erveus, Sigröd, Falun
Esklund, Alf, Solna
Granath, Ulla, Harnosand
Gronvall, Herman, Kristianstad
Hedbeck, Krister, Borås
Hjortzberg Nordlund, Ulla, Goteborg
Holm, Klas Krister, Falköping
Holm, Stig, Goteborg
Holmberg, Åke, Stockholm
Jahnberg, Peder, Gävle
Kassman, Ture, Arvika
Kronning, Eric, Skellefteå
Laurent, Ulla, Uppsala
Magnusson, Loftur, Örebro
Malmquist, Folke, Goteborg
Mattsson, Ragnar, Goteborg
Nordlow, Waldemar, Vanersborg
Nylander, Ulf, Gävle
Olsson, Gunvor, Goteborg
Palm, Erik, Lund
Rehn, Nils O , Södertälje
Rendahl, Carl Ilmar, Stockholm
Rexed, Ursula, Saltsjöbaden

Ribbing, Kerstin, Linköping
Rosengren, Bengt, Goteborg
Rundqvist, Nils, Karlstad
Sahlstrom, Ingvar, Stockholm
Sjogren, Henrik, Jonköping
Suurkula, Juri, Goteborg
Tornquist, Ragnar, Örebro
Wadensten, Lars, Hudiksvall
Wolff, Herbert, Linköping
Wranne, Ingrid, Uppsala
Wulff, Björn, Stockholm
Österlin, Sven, Malmö
Österlind, Göte, Malmö

Norway

Askelund, Per, Trondheim
Aulie, Karl, Kongsberg
Bergaust, Björn, Oslo
Bertelsen, Torstein, Bergen
Birkeland, Hanne, Oslo
Bjerke, Otto, Elverum
Blomskold, Gustav, Narvik
Bore, John, Haugesund
Braathen, Harald, Bergen
Braathen, Sverre Johannes, Stavanger
Bulie, Tore, Oslo
Christensen, Gunnar E , Fredrikstad
Davanger, Martin, Oslo
Egge, Kjell, Hamar
Eitrem, Egil, Tonsberg
Engesæter, Ludvig, Trondheim
Flage, Tor, Oslo
Foss, Björn, Oslo
Gjessing, Harald G A , Drammen
Granaas, Alf Hans, Kristiansand S
Gaarder, Ole, Oslo
Hansen, Egill, Oslo
Hetland Eriksen, Jens, Oslo
Holst, Hans J , Oslo
Holst, Johan Collett, Oslo

recorded in 47 patients (2.5 per cent) 25 mm Hg or higher and in 18 patients (0.96 per cent) 30 mm Hg or higher. The highest pressure value measured was 54 mm Hg. No patient under 45 years of age had a pressure of 30 mm Hg or higher recorded while only two under 45 had a screening value of 25 mm Hg or higher. In the groups with screening values of 25 mm Hg and of 30 mm Hg 70 per cent were over 65 years of age.

The recorded incidence (2.5 per cent) of pressure values of 25 mm Hg or higher is lower than the corresponding results reported in the literature from ophthalmic practices for patients over 40 based on the same screening level (Schiotz weight tonometry). In these reports the incidence values ranged between 3 and 5 per cent (Table 1 - Reed & Bendor-Samuel 1957 Porter 1958 Bendor Samuel *et al* 1960).

In population examinations the incidence of high pressure values is as might be expected lower than among patients in an ophthalmic practice. Stromberg (1962) for instance found 0.95 per cent with pressure values above 26 mm Hg (Schiotz) while Hollows & Graham (1966) saw 1.2 per cent with pressure values of 25 mm Hg or higher (applanation).

It is seen in Table 4 that pressures of 20 mm Hg or higher rose in frequency with increasing age. For patients in the age classes of 35-44 and 45-54 the incidence was 4.5 and 4.1 per cent respectively while the age class of 55-64 showed a rise to 8.4 per cent and finally that of 65-74 a further rise to 16.8 per cent.

For the pressure levels ≥ 22 mm Hg ≥ 25 mm Hg and ≥ 30 mm Hg the incidence was likewise seen to rise with increasing age though with the highest rise in the age class of 65-74.

There was thus found a particularly pronounced rise in the incidence of high pressure values about the age of 60 as also pointed out by Stromberg (1962) and since recorded in various other series examined (Goedbloed 1961 Wright 1966 Hollows & Graham 1966 Bjornsson 1967 Nørskov 1970 and among others).

Pressures above the screening level were more frequently measured among females than among males 9.7 and 7.7 per cent respectively a difference which also prevailed within the individual age groups.

A similar higher incidence among females has been found in two population series (Stromberg 1962 and Hollows & Graham 1966) but has also been recorded in relation to other examinations (Goedbloed 1961 Armaly 1965 and others).

However in the series under review pressure levels ≥ 22 mm Hg ≥ 25 mm Hg and ≥ 30 mm Hg were more frequent in principle among the males. A similar higher incidence among males has been recorded for other series of patients from ophthalmic practices (Ascher 1962 Bjornsson 1967).

This deviation may possibly be related to the special recruiting of patients



Harald G A Gjessing

Harald Gustav Antonio Gjessing M D died on April 6th 1970 without any previous illness

Gjessing was born in Drammen Norway on August 31st 1882 where he grew up and spent most of his life At the grammar school in Drammen he acquired the interest in classical languages which he always kept up After graduating in medicine in 1902 he served as general practitioner in many parts of Norway and also had several hospital appointments

After having spent some time in the eye department of Rikshospitalet, Oslo and in eye departments in Vienna he set up as practising ophthalmic surgeon in Drammen and remained there ever since His M D he obtained in 1920 by a paper entitled Clinical Studies on the Lens Gjessing went on innumerable study tours to most countries of Western Europe and to USA He attended a large number of ophthalmological congresses and gave a good deal of lectures abroad During his travels he made many acquaintances and always took the opportunity to spread knowledge concerning Holth's iridocyclitis

His intense interest in his own discipline is borne out by more than 100 publications mainly on glaucoma and a possible antagonism between cataract and senile macular degeneration In 1950 he published a major paper on Diagnostic and Differential Diagnostic Aspect in Diseases of the Eye

Gjessing became completely absorbed in whatever he undertook and this enthusiasm made him an excellent narrator to whom it was a pleasure to listen

He had been president of the Drammen Medical Association the Oslo Ophthalmological Society and the Norwegian Ophthalmological Society More over he was member of several foreign societies member of honour of the Ophthalmological Society of Copenhagen the Medical Society of Drammen and of the Norwegian Ophthalmological Society In 1962 he was awarded the Norwegian Order of Merit

Birger Walling

Table 5

Reasons for consulting ophthalmologist of 169 screening positive patients and 5 patients who later had the glaucoma diagnosis established

	Distribution of 169 screen ing positive patients	Distribution of 5 patients who had the glaucoma diagno sis established
Request for glasses	59	91
Conjunctival complaints	29	13
Conjunctival complaints during several years	18	9
Impaired vision	16	9
Headache	6	4
Rainbow rings or blurred vision	2	7
Presence of venous thrombosis	8	4
Request for pressure measurements in cases of familial occurrence of glaucoma	2	-
Cataract control	3	2
Referred by general practitioner as part of medical examination	7	0
Sundry causes (e.g. entropion, pterygium, mouches volantes)	17	4

- all signs and symptoms of glaucoma at a fairly advanced stage - which relatively most often led to a diagnosis of glaucoma

The results of this investigation are thus in agreement with the current view that the information given by the individual patient on subjective troubles cannot be expected to contribute towards an early diagnosis of simple glaucoma.

Nevertheless we must realize that the patients in the series under review were selected in as far as they had all desired contact with an ophthalmologist. In this connection it is worth mentioning that on a glaucoma screening by applanation tonometry among members of the volunteer donor corps of Falster had the two donors with visual field defects recorded consulted the ophthalmologist spontaneously within the same period (Norskov 1962).

Familial Predisposition

Occurrence of primary glaucoma among relatives is, according to Waarden

of these latter died within the observation period and nine failed to appear despite written requests being unwilling to any form of examination Finally in four cases examination was given up owing to a poor general condition or high age In no more than one of these cases – a woman aged 86 – were positive data available in support of the glaucoma diagnosis (glaucomatous optic disc)

Results

Grounds for Consulting an Ophthalmologist

It is a commonly held view that where the early diagnosis of simple glaucoma without field loss is concerned we cannot expect to be aided in singling out the glaucoma suspects on the basis of the reason given for consulting an ophthalmologist because patients may be inclined to delay consultation even after glaucomatous field loss

As however it is a question of great interest whether certain lines can be laid down from the data stated by the patients table 5 gives a survey of the 169 screening positive patients reasons for consulting an ophthalmologist

It is plain to see that such a survey yields no direct aid towards singling out the glaucoma suspects nearly two thirds having attended with the traditional complaints – conjunctival troubles or a request for new glasses

Among the patients under 45 years of age conjunctival troubles were the most frequent complaints while half of the patients in the age group of 40–64 had problems with their glasses With a single exception the patients complaining of impaired vision were over 65 There was no difference in principle between males and females

Table 5 also shows the distribution of the 75 patients who after the further examinations had the glaucoma diagnosis established (see p 853) It is seen that in this group too conjunctival complaints and a request for other glasses constituted a scant two thirds of the reasons for consulting an ophthalmologist

A similar preponderance of these two main causes of consultation among patients with simple glaucoma has been recorded by Touvinen (1961) Kata visto (1964) and Gassler (1965) A report made by Leydhecker (1968 a) for patients with gonioscopically open chamber angle showed that 60 per cent had no complaints while 40 per cent had symptoms In 23 per cent of the latter the majority within the group having the highest pressure level these symptoms corresponded to the prodromal ones in closed angle glaucoma

In the present investigation it was in fact rainbow rings around the light presence of central vein thrombosis of one eye headache and impaired vision

Routine tonometry among fairly young patients has also been recommended (Ascher 1962 Becker & Shaffer 1965)

It is difficult to say to which extent routine tonometry is carried through on the lines laid down Porter (1958) on inquiry among American ophthalmologists arrived at the result that 60 per cent of the 170 ophthalmologists asked employed routine tonometry Shapiro & Levine (1966) on the other hand and others noted a considerable slackness on this point among ophthalmologists

However only few ophthalmologists have at an early point of time expressed direct misgivings regarding the request for routine tonometry in ophthalmic practice (Schmidt 1959 Holm 1960 Ehlers 1960 Lauterstein 1960 1961 1962 1963 Walser 1965)

It is very important that the ophthalmologist who intends to adopt routine tonometry in his private practice be familiar to the greatest possible extent with the problems arising for both patient and doctor in relation to realisation of such a glaucoma prophylactic contribution

It is therefore surprising that as seen in table 1 fairly few papers are available in which an account is given of the experience gained from employment of routine tonometry among patients consulting an ophthalmologist.

In the present paper the results will be reported of a routine tonometry study using applanation tonometry carried out by an ophthalmologist in connection with glaucoma screening undertaken on the Island of Falster during the years 1960-1963

Present Investigations

The investigation comprised patients aged 35 or older from the Island of Falster who within the period from October 1 1960 to February 28 1962 consulted the only ophthalmologist of the island (E. Westerlund MD)

The only patients ruled out from the start were those with previously recognized primary or secondary glaucoma

Applanation tonometry concluded the eye examination otherwise concentrating on the cause of the patients consulting the ophthalmologist. The measurements were performed between 12.30 and 5 p.m.

Just over half of the applanation measurements (61 per cent) were undertaken by the author and the remaining by one other examiner

The series comprised 2079 patients. In table 2 we see the age and sex distribution related to that for the population of Falster (46 662 inhabitants in census September 7th 1960). The patients within the age groups of 40-64

in arranging a recording of the 24 hour pressure variations to establish the glaucoma diagnosis. Especially it is difficult to carry through the morning measurement. Problems will also arise when the distance between ophthalmologist and patient is so great that admission to hospital for the purpose of regular recordings is contemplated.

Of the patients in the series under review 55 had the 24 hour variations recorded during stay in the ophthalmic unit. Three fourths of these were subjected to applanation tonometry by the same examiner while for practical reasons the remainder had measurements carried out by two skilled nurses using Schiotz weight tonometer (7.5 g).

The times of the maximum pressure values measured in the 55 patients have been set out in table 6. The last control value measured in the ophthalmic consultation was compared with those recorded within 24 hours of admission 11 a.m. - 4 p.m. 6-8 p.m. 7 a.m. and 8-10 a.m. In the cases where the same maximum pressure value was measured at different times within the 24 hours the respective times were included. It is seen in table 6 that the maximum value most often was measured in the ophthalmic consultation even compared to the total number of measured values plotted along the 24 hour curve. The morning measurements were the second in frequency to give maximum pressure values whereas in rare cases only was a maximum pressure value recorded in the evening.

A different way of assessing the relation between the out patient control pressure measurement and the 24 hour measurements during stay in hospital is that of determining the distribution of the values of 25 mm Hg or higher which according to the chosen criteria contribute largely towards establishing the diagnosis of glaucoma.

Pressure values of 25 mm Hg or higher were measured in a total of 61 eyes (41 patients). In 39 of these (24 patients) such values were obtained both by

Table 6
Recording of times for maximum pressure values in 55 patients (109 eyes). The 24 hour values measured during the first 4 hours stay in hospital are compared with the last control values in ophthalmic practice.

ophthalmic practice	during stay in hospital			
	11 a.m. - 4 p.m.	6 - 8 p.m.	7 a.m.	8 - 10 a.m.
150	14	1	23	15

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ROUTINE TONOMETRY IN OPHTHALMIC PRACTICE

I Primary Screening and Further Examinations for Diagnostic Purposes

BY

KNUD NØRSKOV

Within the past 15-20 years great efforts have been made to intensify the glaucoma prophylactic work by screening using tonometry carried through on different population groups (reviews by Leydhecker 1960 Ourgaud & Étienne 1961 Yusupov & Sumatokhina 1963 Posner & Fogland 1964 Segal & Skwierczynska 1967 and Pollack 1968)

A not previously recognized primary glaucoma is generally stated to have been disclosed in between 1.5 and 2 per cent of the examined persons aged over 40. In such examinations we operate with an arbitrary glaucoma concept which is based on the chosen glaucoma criteria but does not distinguish between presence of ocular hypertension and glaucoma with glaucomatous field loss.

This is the background of the frequently advanced claim for routine tonometry of all patients aged 40 or older consulting ophthalmic medical practitioners no matter whether the eye examination raises suspicion of glaucoma (Phelps 1949 Hildreth & Becker 1957 Sloan 1957 Reed & Bendor Samuel 1957 Porter 1958 Sloan 1959 Leydhecker 1959 Bendor Samuel *et al* 1960 Schmidt 1960 Bruens 1961 Ascher 1962 Corydon Andersen 1964 Fronimo poulos *et al* 1965 Björnsson 1967 among others)

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burg *et al* (1961) to be expected in 17-18 per cent Westerlund (1947) in a Danish study found a percentage of 13

The patients included in the present investigation were not questioned about a familial predisposition in relation to the routine tonometry but such a questioning was carried through for the 169 patients with a screening pressure above 20 mm Hg. A predisposition among near relations was found to exist in the families of eight patients (4.7 per cent) in five of whom a diagnosis of glaucoma was subsequently established.

Pressure Control

In fixing an intra ocular pressure level for the individual patient we must bear in mind that as stated previously the estimation was based on a varying number of measurements distributed over control measurements in ophthalmic practice and measurements during out patient examination or stay in ophthalmic unit.

In 56 patients (94 eyes) or 33.1 per cent of the 169 screening positive repeated pressure measurements gave 25 mm Hg or higher in support of the glaucoma diagnosis while in 23 patients (36 eyes) pressures of 30 mm Hg or higher were recorded on repeated measurements.

For 111 patients (221 eyes) the results of control pressure measurements in ophthalmic practice were available. This afforded a possibility of comparing screening pressure with control pressure measured at the same time of the day (between 1 and 5 p.m.) in order thus to get an impression of the consequences it would have for the patients concerned if on the basis of the same screening level of 20 mm Hg the control measurements had been chosen as the normative examination.

In 13 or 11.7 per cent of the 111 patients the pressure values on the control examination were under the screening level in both eyes. These cases would accordingly have been missed on a glaucoma screening based on the control pressure measurements.

In two of these 13 patients a diagnosis of glaucoma (without field loss) was however subsequently established on the basis of the further examinations for diagnostic purposes. This emphasizes the fact that by screening based on a single measurement we must not forget that glaucoma cases may be missed.

It will furthermore be a commonly employed procedure in such cases as the 13 with a control tension below the screening level to characterize these values as false positive issues of the primary screening. However the results of the present investigation showed the risk involved in refuting on the basis of a single control measurement a suspicion of glaucoma raised on routine tonometry.

The ophthalmic medical practitioner will not infrequently have difficulty

Table 2

Age and sex distribution of patients who consulted ophthalmic medical practitioner within the period from October 1 1960 to February 28 1967 seen in relation to the population of Falster

		25-39	40-64	≥ 65	Total
Population of Falster census 96 9 1960	males	3975	7391	2810	23715
	females	4218	7943	3154	23447
	Total	8143	14637	5964	46662
		5-39	40-64	≥ 65	Total
Ophthalmic practice	males	51	484	211	746
	females	102	838	343	1283
	Total	153	1322	554	2029

and within that over 65 represented 9 per cent of the total number of inhabitants within the age groups concerned. At the census the age group of 40-64 and that over 65 included 51 and 47 per cent males respectively. In the corresponding age groups of patients from the practice males constituted 37 and 38 per cent respectively. The attendance was thus greater among females than among males as is often seen in an ophthalmic practice (Bjornson 1967; Norislov 1970b).

Infectious eye diseases among others prevented tonometry in the cases of 9 patients (57 males and 45 females). In another 50 patients (19 males and 31 females) tonometry could not be carried through owing to nystagmus, corneal changes or inadequate co-operation.

Thus 1897 of the 2029 attending patients or 92.8 per cent (males 90.5 per cent - females 94.1 per cent) were subjected to the routine tonometry aimed at. The age and sex distribution is shown in table 3.

None of the remaining 147 patients displayed signs of glaucoma.

Screening Level

It had been decided that an applanation value of 20 mm Hg or higher in one or both eyes and a difference of 4 mm Hg or more between the two eyes motivated further examinations with a view to presence of glaucoma.

Table 7
Distribution of 163 screening positive patients (53 eyes) according to appearance of optic disc and visual field

Visual field	BY ITHALMOSCOPY				
	normal	suspected glaucomatous	glaucomatous	not estimated	Total
1 normal	237	7	-	-	244
2 barring of the blind spot	8	4	4	-	16
3 arcuate scotoma without peripheral break through	-	1	4	-	5
4 arcuate scotoma with peripheral break through	-	-	-	-	-
5 defects in nasal quadrants	-	1	2	-	3
6 loss of visual field in two or more quadrants	-	-	3	-	3
7 central retinal island or total blindness	55	3	2	4	64
8-7 visual field test not carried through	300	16	15	4	335

Table 1

Review of previous routine tonometries carried through in ophthalmic practices

	number	age	screening level calibration table Schiotz	suspects %	GLAUCOMA DETECTED (PREVIOUSLY UNKNOWN)							
					with glaucoma field loss %	without glaucoma field loss %	Total %	boderline cases %				
Phelps (1949)	720	> 45	< 3/5 5 27 mm Hg (1948)	-	18	25	19	26	37	51	-	-
Vaughan et al (1957)	5528	> 40	> 25 mm Hg (1948)	-	-	-	-	-	122	20	-	-
Hildreth & Becker (1957)	2000	> 40	-	49	-	-	38	19	38	19	-	-
Reed & Bender Samuel (1957)	2000	> 40	≥ 25 mm Hg	99	28	14	30	15	58	29	7	0.4
Sloan (1957)	1184	≥ 40	≥ 26 mm (1954)	46	-	-	-	-	31	26	12	10
Corydon Andersen (1958)	600	> 50	≥ 22 mm Hg (1952)	18	-	-	-	-	8	10	10	13
Lortier (1958)	987	≥ 40	-	31	-	-	-	-	28	28	-	-
Lortier (1958)	2000	> 40	≥ 25 mm Hg (1954)	61	22	11	22	11	44	22	-	-
Sloan (1959)	2100	≥ 40	≥ 26 mm Hg (1954)	77	-	-	-	-	45	21	30	14
Bender Samuel et al (1960)	5000	> 40	≥ 25 mm Hg	249	32	06	43	09	75	15	-	-
Holmes (1961)	2000	≥ 40	-	-	-	-	-	-	23	12	-	-
Ascher (1962)	1000	≥ 21	≤ 4/5 5 (1955)	40	10	10	19	19	29	29	-	-
Gassler (1965)	3000	20-85	< 2 5/5 5 (1955)	33	-	-	-	-	98	33	-	-

24-hour measurements and in ophthalmic practice In the remaining 12 eyes (10 patients) values of 25 mm Hg or higher were recorded in the 24 hour pressure curve whereas the consultation values were below 25 mm Hg

In 10 eyes (7 patients) the reverse was the case the consultation values being here 25 mm Hg or higher and the 24-hour pressure level recorded below 25 mm Hg

The stated results suggest that the ophthalmologist by basing his opinion on the out-patient control pressure values measured within the ordinary consultation hours is in a better position to establish the glaucoma diagnosis than might be expected considering the fact that maximum values are stated relatively rarely to be recorded within the interval from 12 o'clock to 6 p.m. the period during which the ophthalmic medical practitioner frequently sees his patients (Hager 1958 Drance 1960 Katavisto 1964)

This holds good when the pressure measurements are carried through under uniform external conditions The unexpected result in the present study is perhaps due to the measurements having not taken place under uniform external conditions the 24 hour measurements having been performed during stay in hospital where the tension might be expected to fall to a lower level than when the patient is in his usual environment (Hager 1958 Goldmann 1960 Ourgaud & Étienne 1961 Katavisto 1964)

In the cases of 87 patients it was however possible to compare a morning measurement (between 8 and 10 a.m.) during an out patient examination in the ophthalmic clinic with an afternoon measurement in the ophthalmic consultation both carried out under uniform external conditions As might be expected the pressures measured at 25 mm Hg or higher rose in number from afternoon measurement to morning measurement namely from 8 to 16 eyes This result is in agreement with the current view that maximum pressures often are recorded at a point of time which is not within the usual consultation hours

Ophthalmoscopy

Table 7 shows the conditions of the optic discs estimated for 331 eyes (three patients were one eyed while in four cases ophthalmoscopy was impossible owing to cataractous changes)

The discs were normal in 300 eyes while in 15 it was glaucomatous and in 16 a glaucomatous disc was suspected

Ten patients or 5.9 per cent of the screening positive had a glaucomatous disc of one or both eyes while twenty had either a glaucomatous disc or one suspicious of glaucoma These constituted 11.8 per cent of the 169 patients subjected to further examination or 1.1 per cent of the 1882 subjected to routine tonometry The percentage number is considerably smaller than in

pressure otherwise is within the normal range has been of no importance in the establishment of the glaucoma diagnosis

It rather seems that on demonstrating tension differences in patients with values otherwise within the normal range one should in the first place aim at precluding errors of measurement (Leydhecker 1958 Jervey 1962)

Patients with Applanation Values Above the Screening Level

169 patients or 9.0 per cent of the 1882 subjected to tonometry had applanation values measured of 20 mm Hg or higher. The grouping was based on the eye for which the highest intra ocular pressure was recorded.

The distribution according to age, sex and pressure level is seen in table 4. In 89 patients (4.7 per cent) applanation values of 22 mm Hg or higher were

Table 4
Age and sex distribution of 169 patients with applanation value above the screening level

		35-44	45-54	55-64	65-74	75-84	≥ 85	Total	%
		377	557	406	409	185	70	1882	
≥ 0 mm Hg	males	5	4	7	11	17	2	56	7.7
	females	17	20	27	35	22	1	112	9.7
	Total	22	24	34	46	39	3	169	-
	%	4.5	4.1	8.4	16.8	20.7	-	9.0	-
≥ 1 mm Hg	males	4	7	4	17	14	2	38	5.6
	females		10	9	15	13	1	51	4.2
	Total	4	12	13	32	27	3	80	-
	%	1.1	1	3.2	9	14.3	-	4.7	-
≥ 2 mm Hg	males	7	1	2		6	1	19	2.8
	females	-	5	4	17	11	1	38	2.3
	Total	2	6	6	19	12	2	41	-
	%	0.55	1.0	1.5	6.2	6.4	-	2.5	-
≥ 3 mm Hg	males		1	1	5	7	-	9	1.3
	females		2	1	4	7	-	7	0.7
	Total		3	2	9	14	-	16	-
	%		0.5	0.49	2.9	2.1	-	0.96	-

Table 7
Distribution of HJ screening positive patients (335 eyes) according to appearance of optic disc and visual field

Visual field	Ophthalmoscopy				Total
	normal	suspected glaucomatous	glaucomatous	not estimated	
1 normal	237	7	-	-	244
2 barrier of the blind spot	8	4	4	-	16
3 arcuate scotoma without peripheral break	-	-	-	-	-
4 thin cup	-	1	4	-	5
5 arcuate scotoma with peripheral break through defects in nasal quadrants	-	1	2	-	3
6 loss of visual field in two or more quadrants	-	-	3	-	3
7 central retinal artery or vein blindness	55	3	2	4	64
8-9 visual field test not carried through	-	-	-	-	-
10-11 visual field test not carried through	300	10	15	4	329

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THE FREQUENCY OF POSITIVE DYE TEST IN BLIND CHILDREN

BY

MARIT LANGSET TORE MIDTVEDT and TOV OMLAND

Congenital and acquired systemic toxoplasmosis has been diagnosed with increasing frequency in recent years. The classical signs of congenital toxoplasmosis i.e. hydrocephalus, intracranial calcifications and chorioretinitis are well known. Recent work however suggests that the most common form of congenital toxoplasmosis is that in which only the eyes are involved (Fair 1961). Ocular manifestations may also complicate acquired systemic toxoplasmosis (Hogan 1961, Perkins 1961, Rieger 1962, Ramsell & Gamero 1967).

Thus the eye seems to be one of the predilection places for *Toxoplasma gondii*. If so this might be reflected in a higher frequency of positive dye test (DT) in blind individuals than in the normal population. The present investigation shows the frequency of positive DT in a group of blind school children.

Material and Methods

Sera were taken from all children at the Dalen State School for the Blind Trondheim, Norway. The children were from various districts of the country.

and were all within the age group 7-14 years. Their visual acuity varied from complete blindness to 20/60.

DT results from children in different departments at Rikshospitalet, Oslo, Norway, and from school children living in the southern part of Norway were employed as a comparison group. This material has been described in detail elsewhere (Midtvedt 1965).

The DT technique used was as described in previous papers (Grondahl, Midtvedt & Kolstad 1962; Midtvedt 1965).

Results and Discussion

Table 1 presents the frequency of positive DT and the titre values in blind children. In the age group 7-10 years, 47 per cent show positive DT compared with 52 per cent in the age group 11-14 years. In both age groups the titre values were low (1:4 or 1:10 in more than 80 per cent of the cases), particularly in the older group. In the normal population the frequency of positive DT increases with age during childhood, and the majority of the values is above 1:10 (Midtvedt 1965). The present findings might indicate that the blind children have been infected at an earlier age than those in the control group.

Table 2 shows the frequency of positive DT in blind children as compared to the findings in a control group. The data obtained permit a comparison by the χ^2 test ($p < 0.001$). The test supports the assumption of a considerably higher frequency of positive DT in blind children than in the control group.

It should be mentioned that only one of the blind children was previously diagnosed as a case of toxoplasmosis. No further attempts were made to corre-

Table 1
The frequency and titre values of positive DT in blind children

Age in years	No. of	No. of positive	Per cent of positive	Titre			
				1:4	1:10	1:40	1:200
7-10	30	14	47	6	4	3	1
11-14	29	15	52	10	5	0	0
Total	59	29	49	16	9	3	1

other series from ophthalmic practices where from one fourth to one third of those subjected to further examination presented disc changes (Porter 1958 Ascher 1962 Bjornsson 1967)

The two youngest patients with a glaucomatous disc were 57 and 59 years old respectively while the other patients were over 65

The youngest patient with a glaucoma suspicious disc was 41 years old

Visual Field Measurements

The measurements were carried through by campimetry using object sizes 2/2000 6/2000 and also 17/2000 if required In a few instances the campimetry was supplemented by measurement with Pflüger's perimeter

Of the 169 patients (335 eyes) only 141 had visual field measurements carried through of one or both eyes (271 eyes) Seven patients had died prior to control examination and nine were unwilling to continue examination while 12 (7.1 per cent) could not have a sufficiently accurate visual field measurement carried through Finally in the cases of nine eyes an estimation was forborne owing to presence of other disease — mainly cataract

The results of the visual field measurements are seen in table 7 The visual field was normal in 244 cases while visual field defects were observed in 27 eyes Pronounced visual field defects were present in no more than 11 of the latter

A total of 19 patients or 11.2 per cent of the screening positive had visual field defects of one or both eyes but extensive defects were seen in only eight of these 4.7 per cent)

The youngest patient with pronounced visual field defects was 48 years of age The remaining with grave visual field defects were aged over 65

Table 7 also shows the relation between the appearance of the optic disc and the result of the visual field measurement It is seen that all the eyes with a glaucomatous disc that were subjected to visual field measurement also presented a visual field defect Among these were five of the six cases with the gravest visual field defects

In half of the eyes whose disc was characterized as glaucoma suspicious the visual field was normal while the others had visual field defects mainly group 2

In eight eyes with discs characterized as within the normal range beginning visual field defects were disclosed (group 2) These consisted in all cases in barring of the blind spot with associated depression of the margins in the upper quadrants at object size 2/2000 Only two eyes also showed visual field defects at object size 6/2000

Gonioscopy

Gonioscopy was carried through on 147 patients who were grouped in con

This procedure was chosen not only to attain to an overall evaluation of the problems relating to employment of routine tonometry in ophthalmic practice but also because it was found difficult as carried through by Hildreth & Becker (1957) to definitely delimit a group of patients who after ocular examination without routine tonometry would be without suspicion of glaucoma

In the endeavours to increase the effectiveness by employing routine tonometry and thereby reduce the number of missed glaucoma cases a tendency has manifested itself in the course of years towards using a lower screening level (Hunt 1966 Pollack 1968 Nørskov 1970 a)

In agreement with this a screening level of 20 mm Hg was chosen using applanation tonometry This involved however that every 11th patient (9.0 per cent) was suspected of glaucoma on this basis alone This is a considerably higher percentage than stated for any of the series from ophthalmic practice mentioned in table 1 In these the percentage numbers of screening positive ranged between 2 and 5 However as stated previously a direct comparison of these series is impossible

In this connection there may be reason to mention a calculation undertaken by Pollack (1968) on the basis of 18 screenings comprising 217 000 individuals He arrived at the result that with a screening level of 20 mm Hg routine tonometry gave 12 per cent screening positive Compared with this the incidence in the series under review is by no means unrealistic especially not when one considers that the series consisted of patients from an ophthalmic practice

Proposals

Regarding Alterations of the Screening Procedure to Reduce the Number of Patients Referable to Further Examination

The very considerable number of screening positive patients when a screening level of 20 mm Hg is employed tempts one to choose a higher screening level

In this connection it is important to have the most exact knowledge possible of the relation between an alteration of the screening level and the number of glaucoma cases consequently missed

In the series under review alterations of the screening level to 21 mm Hg 22 mm Hg and 25 mm Hg respectively would have reduced the number of patients referable to further examination to 73.53 and 28 per cent respectively of the original 169 with a screening pressure value of 20 mm Hg or higher At the same time the number of missed glaucoma cases when using the criteria stated p. 853 would have constituted 9.16 and 47 per cent respectively of the original number of diagnosed glaucoma cases

Another solution might be that of graduating the screening level according

formity with the simplified classification employed by Gorin & Posner (1957) a wide open chamber angle is characterized by the entire trabecular network as well as the ciliary body being visible. The chamber angle is characterized as open when only the trabecular network is visible but the ciliary body is either not visible at all or seen as a narrow band. Finally the chamber angle is described as narrow when neither the ciliary body nor the posterior two thirds of the trabecular network is visible. The chamber angle is closed when its structures behind Schwalbe's line are invisible.

The grouping based on the appearance of the chamber angle and the patients' ages is shown in table 8. It is seen that in 39 per cent (51 patients) the chamber angle was wide open, in 44 per cent (61 patients) it was open and in 17 per cent (23 patients) narrow. In no more than two patients did gonioscopy show a closed chamber angle.

This distribution does not differ essentially from the statements for normals. Thus Shaffer (1960) and Pietruschka (1959) found the percentage number of persons with a narrow chamber angle to be 12 and 15 respectively. In drawing comparisons attention must however be given to differences regarding the basis of the classification in the series concerned.

The number of individuals with a narrow chamber angle will rise with increasing age (Leydhecker 1960, Duke Elder 1962).

In the series under review 11 per cent (four patients) in the age group of 35-54 had a narrow chamber angle against 19 per cent (21 patients) in that over 55.

Table 8
Gonioscopy Distribution according to appearance of chamber angle and patients' ages

	35-54		≥ 55		Total	
	number	%	number	%	number	%
wide open angle	15	30	41	40	57	39
open angle	20	34	45	41	65	44
narrow angle	4	11	19	19	23	17
closed angle	-	-	2	2	2	1

to age. Thus 21 mm Hg has been suggested for the age class of 20-39, 22 mm Hg for that of 40-59 and 24 mm Hg for that of 60-79 (Pollack 1968).

If in the present investigation we chose on the same lines to alter the screening level to 22 mm Hg for patients between the ages of 35 and 64 and to 25 mm Hg for patients over 65, the number of patients within the two age groups referable to further examination would fall to 39 per cent (35-64 years) and 35 per cent (over 65) of the original 169 patients with a screening pressure of 20 mm Hg or higher. At the same time the number of false negative cases would constitute 24 per cent (35-64 years) and 44 per cent (over 65) of the original number of diagnosed glaucoma cases.

If we adopt the procedure of graduating the screening value we must also consider an adjustment according to the patient's sex and the time of the screening tension measurement.

The results of the present investigation thus give plain evidence of our dilemma: as employment of a higher screening level possibly graduated according to age, sex and time of the day does give a welcome reduction of the number of patients referable to further examination but at the expense of missed glaucoma cases judged by the glaucoma criteria chosen.

A procedure frequently employed for lessening the efforts required after routine tonometry is that of letting the result of a single control measurement decide whether more time consuming further examinations are to take place.

If this procedure had been employed in the present study it would have been possible to rule out 12 per cent of the 111 patients who had the tension controlled within the same period of the day. However, the further examinations revealed that such a procedure would result in missed glaucoma cases which in fact had been disclosed at the initial routine tonometry.

How Can the Ophthalmologist Disclose Glaucoma Cases With No Glaucomatous Field Loss Without Employing Routine Tonometry?

In relation to the present study, the results of which plainly show the enormous work with which the ophthalmologist adopting routine tonometry is charged, it seems reasonable to deal with the other chances the ophthalmologist has of tracing glaucoma before glaucomatous field loss has set in.

The patient's history in its widest sense, the central visual acuity, ophthalmoscopy and visual field measurement are at the ophthalmologist's disposal for this purpose.

In cases of closed angle glaucoma, valuable anamnestic data are often available but to judge from the present investigation we cannot expect much aid from the information given by patients with simple glaucoma concerning the cause of their application, at any rate not till the patient suffers from glaucoma with field loss.

Provocative Tests

A Water provocative test 135 patients (269 eyes) or 80 per cent of the 169 screening positive were subjected to water provocative test. Of the 34 patients who did not have this test carried through six had the diagnosis established otherwise while five objected to the test and in three cases the test was forborne owing to the patients poor general condition. In the remaining cases no further examination was undertaken in the ophthalmic unit. Seven patients were unable to drink a whole litre of water. A rise of 8 mm Hg or higher was obtained in 55 eyes corresponding to 20.4 per cent of the water provocative tests carried out. Of the subjects reacting positively to the test 75 per cent were over 65 years of age.

A detailed account of the experience gained from the water provocative test in the present series of screening studies has been given in a previous report (Nørskov 1967 a).

B Priscol provocative test This provocative test was only offered to patients admitted to the ophthalmic unit. It was carried through for 36 (68 eyes) of the 62 hospitalized patients.

Rises of 11 mm Hg or higher were released in 28 eyes or 41.2 per cent. Details concerning the results of the present investigation have been given in a previous publication (Nørskov 1966).

C Pupil dilatation tests The mydriasis tests held no central position in the present work which concentrated on tracing simple glaucoma by routine tonometry. Such tests were preferably carried through on patients staying in hospital thus on a total of 40 patients in relation to pupil dilatation for retinal photography (cyclogyl (cyclopentolate) or homatropine 1 %).

Finally a dark room test was available for two patients – in both with a negative result.

In ten patients whose chamber angle was characterized as narrow the test gave no pathological alteration. A rise of 8 mm Hg or higher was released in three (six eyes) of the 30 patients with open or wide open chamber angle. The maximum rise was 17 mm Hg.

These reactions to pupil dilatation despite a gonioscopically open chamber angle must be regarded as unusual though such have been recorded by various writers (Leydhecker 1955 Galin 1961 Harris 1968).

Simple Glaucoma

Presence of one or more of the following criteria were required for establishment of the glaucoma diagnosis

- 1 Distinct marginal cupping of the optic disc
- 2 Reproducible glaucomatous visual field defects

If further on the basis of our knowledge concerning the relationship between glaucoma and central vein thrombosis glaucoma and diabetes, glaucoma and high myopia glaucoma and thyroid dysfunction as well as glaucoma and pseudo exfoliation as suggested by Becker & Shaffer (1965) we aim at utilizing the histories to suspect glaucoma in such cases then 25 patients or 15 per cent of the 169 caught by routine tonometry would have been suspects. Of these 16 patients or 21 per cent of the 75 newly diagnosed glaucoma cases subsequently had the glaucoma diagnosis established.

Another eight patients gave information on a familial predisposition to glaucoma. The diagnosis was established in five or 6.7 per cent of the 75 diagnosed glaucoma cases. In Leydhecker's (1959) and Bertelsen's (1965) series glaucoma occurred among near relations in 8.2 and 13 per cent respectively of the patients with diagnosed glaucoma.

There seems in other words to be a certain possibility of rendering the work with glaucoma tracing more efficient by utilizing the anamnestic data on the stated lines.

Impaired central visual acuity caused by glaucoma occurs only at an advanced stage of the disease but this may in certain cases give occasion to disclosure of glaucoma without field loss of the other eye.

Ophthalmoscopy is the earliest examination employed for glaucoma screening. Though ophthalmoscopy is rather unsuitable for disclosing glaucoma without field loss many ophthalmologists still regard it as the most important weapon within the field of glaucoma prophylaxis among others (Holm 1960, Colenbrander 1960, Graham & Hollows 1966, Walker 1966, Blaxter 1966).

Use of ophthalmoscopy is however rendered difficult by the gradual transition from physiological to pathological cupping.

It is generally stated that if the cupping covers more than 60–70 per cent of the disc area glaucoma must be suspected (Leydhecker 1960, Snyderker 1964, Becker & Shaffer 1965). In agreement with this a screening based on ophthalmoscopy alone will according to Snyderker (1964) raise suspicion of glaucoma in 4 per cent of persons aged over 40.

However in the present series the incidence was no more than 1.1 per cent and in those of Porter (1958), Ascher (1962) and Bjornsson (1967) 1.0, 1.1 and 1.7 per cent respectively. This seems to indicate that the ophthalmologist who employs both ophthalmoscopy and routine tonometry for screening invariably takes account of the routine tonometry value when evaluating the optic disc. This also explains why in the present study only one glaucoma suspicious disc was found among the subjects with tension values below the screening level. The found percentage of glaucoma suspicious discs thus is no indication of the number of discs giving rise to suspicion of glaucoma when ophthalmoscopy alone is employed for screening.

As visual field measurement usually is not included in an ordinary eye

- 3 Intra ocular pressures ≥ 25 mm Hg
- 4 Rises ≥ 8 mm Hg in response to water provocative test
- 5 Rises ≥ 11 mm Hg in response to priscol provocative test
- 6 Rises ≥ 8 mm Hg in response to mydriasis test
- 7 Rises ≥ 10 mm Hg in response to dark room test

In the cases of 75 patients representing a scant half of the 169 patients traced by routine tonometry a diagnosis of glaucoma was in agreement with this rendered likely in 133 eyes as shown in table 9 where the distribution according to criteria is indicated

In half of the cases only one criterion of glaucoma was present while in

Table 9

Criteria for establishing the glaucoma diagnosis in 133 eyes (75 patients)

1	Criteria present	
	pressure values ≥ 25 mm Hg	37
	water provocative test ≥ 8 mm Hg	18
	priscol provocative test ≥ 11 mm Hg	10
	visual field defect	1
	mydriasis test ≥ 8 mm Hg	1
2	Criteria present	
	pressure values ≥ 25 mm Hg + visual field defect	6
	pressure values ≥ 25 mm Hg + pos water provocative test	24
	pressure values ≥ 25 mm Hg + pos priscol provocative test	8
	pressure values ≥ 25 mm Hg + pos mydriasis test	1
	visual field defect + glaucomatous optic disc	4
	pos water prov test + pos priscol prov test	1
	pos water prov test + visual field defect	2
	pos priscol prov test + visual field defect	2
3	Criteria present	
	pressure values + glaucomatous disc + visual field defect	6
	pressure values + visual field defect + pos priscol prov test	1
	pressure values + visual field defect + pos water prov test	2
	pressure values + pos mydriasis test + pos priscol prov test	1
	pressure values + pos water prov test + pos priscol prov test	1
	pressure values + pos mydriasis test + pos water prov test	1
4	Criteria present	
	pressure values + glau disc + pos mydriasis test + pos water prov test	2
	Criteria present	
	pressure values + glaucomatous optic disc + visual field defect + pos water prov test + pos priscol prov test	3

examination in ophthalmic practice a knowledge of the relation between the appearance of the optic disc and the extent of the visual field defect will be a factor of great importance from a glaucoma prophylactic aspect. Traditionally a fair correlation is claimed to exist between the two variables (Traquair 1933 Harrington 1964) though exceptions have frequently been stated (Aulhorn & Harms 1960 Armaly 1962 Shutt *et al* 1967 among others)

In agreement with this the series under review showed as a main rule a fair correlation between the appearance of the optic disc and the extent of the visual field defect (table 7) but in six patients (eight eyes) barring of the blind spot was found despite normal discs

In making up one's mind about the usefulness of visual field measurement as a primary screening test one must not forget that it is particularly elderly glaucoma suspects who are subjected to this test - in the present series more than half were over 60. Visual field measurement had to be completely abandoned in 7 per cent but this figure by no means reflects the difficulties not infrequently prevailing with regard to making out whether a patient of this age group has a minor visual field defect

Finally in this connection it must be a matter of great interest for the ophthalmologist to realize how many glaucoma cases will be missed by employing a procedure which does not include routine tonometry

According to Hildreth & Becker the missed glaucoma cases constitute 19 per cent in the age group over 40. Other ophthalmologists have arrived at between 1 and 3 per cent missed glaucoma cases dependent on the chosen glaucoma criteria in series from ophthalmic practices

No such grouping has been undertaken of the series under review. Nevertheless we had a possibility of forming an impression of the number of diagnosed cases before the introduction of routine tonometry compared with that after the introduction

During a five year period prior to the introduction of routine tonometry on Falster on an average 78 fresh glaucoma cases were recorded annually while the number of patients with glaucomatous field loss diagnosed annually within the routine tonometry period amounted to 84 annually

This means that without use of routine tonometry few or no glaucoma cases with no field loss will be disclosed while at the same time all with field loss seem to be detected

Reflections in Relation to Further Examinations

The condition that routine tonometry can have the desired glaucoma prophylactic value is that all the patients suspected of glaucoma by this procedure do have further examinations carried through

The request for control examination should therefore be so urgent that the

only 18 eyes (14 per cent) not less than three criteria were available to justify establishment of the diagnosis. In this connection we must however make allowance for the greatly varying frequency of accomplishment for the different methods of investigation.

The criterion most frequently present was that of pressure values recorded at 25 mm Hg or higher which occurred in 94 eyes.

In 58 patients such high values were a bilateral phenomenon while 17 patients had the glaucoma diagnosis established for one eye only. In 12 of these cases the other eye was characterized as a borderline case and in four as normal. One patient was one eyed.

A comparison of the incidence of closed angle glaucoma with that of simple glaucoma showed as might be expected a considerable predominance of the latter form, only two patients having displayed a gonioscopically closed angle.

Table 10 shows the age and sex distribution of the 75 patients. The total number of diagnosed glaucoma cases constituted 40 per cent of the original number of examined patients. The incidence was found to rise with increasing age. No cases occurred in the age group under 40 but the incidence rose from 1.4 per cent in the age group of 45-54 to 3.2 per cent in that of 55-64. The highest rise from 3.2 to 9.0 per cent was noticed from the age group of 55-64 to that of 65-74.

For males and females the diagnosed glaucoma cases constituted 4.2 and 3.9 per cent respectively. The highest rise in number for both males and females was seen from the age group of 55-64 to that of 65-74. Otherwise the distribution varied somewhat within the individual age groups.

Table 10

Age and sex distribution of 75 patients who had the glaucoma diagnosis established

	males		females		Total	
	number	%	number	%	number	%
35-44	2	1.6	2	0.80	4	1.1
45-54	3	0.92	5	1.6	8	1.4
55-64	4	3.0	9	3.3	13	3.2
65-74	11	11.3	17	8.0	28	9.0
75-84	8	8.8	12	12.4	20	10.6
≥ 85	1	(11.1)	1	(9.1)	2	(10.0)
Total	28	4.2	47	3.9	75	4.0

patients concerned really do attend. At the same time however one must take care not to render the patient apprehensive.

In the present study we proceeded by explaining to the patient that the tension in the eye was a little above normal and that on this account we advised control within 1-3 months. However by this procedure 30 per cent failed to appear. Other ophthalmologists have had difficulties of the same kind in their practices. Reed & Bendor Samuel (1957) and Bendor Samuel *et al* (1960) stated that 30 and 38 per cent respectively of their patients failed to attend.

The experience gained from the present investigation goes to show that the number of absentees can be reduced by proposing control after one month at most and preferably at a fixed date. Summoning by letter effected that 82 per cent of the absentees were examined later.

In planning the further examinations we must aim at a reasonable balance between the examinations judged to be necessary for taking a decision on the suspicion of glaucoma raised by routine tonometry and the examinations that are practicable in consideration of work load economy and the patient's psyche.

In arranging the further examinations we originally aimed at a procedure fitting in with the conditions available to the ophthalmologist with no support from an ophthalmic unit. The reasons why hospitalisation was nevertheless employed were partly a desire for rapid accomplishment of the examination in question and partly to render the examination more convenient to the patients living far away from the ophthalmologist.

Many of the patients were however unwilling to accept admission to hospital. As many as one fourth of the patients whose examination had been arranged refused admission.

On the other hand it was often difficult to make the patients who had been through the entire series of examinations accept that the results achieved afforded no basis for any treatment of their eyes.

If however the ophthalmic medical practitioner is to carry through further examinations on the lines stated in the present paper which by no means can be characterized as ideal this cannot be done without a radical change of the usual working rhythm. The consultation hours will have to be prolonged in consequence of the many control pressure measurements and provocative tests and 24-hour pressure measurements cannot take place within the usual consultation hours.

The provocative tests play a prominent role in the diagnosis of glaucoma without field loss. However their use has the definite disadvantage that from a clinical aspect the tests afford no possibility of foretelling which patients are liable to future development of visual field defects.

Regarding tonography different views prevail on the basis of follow up

As shown in table 11 12 patients (eight males and four females) had glaucoma at a fairly advanced stage that is with a glaucomatous optic disc or more extensive visual field defects. These constituted 0·4 per cent of the 1882 subjected to routine tonometry the incidence being 1·2 per cent for males against only 0·33 per cent for females. By way of comparison it may be mentioned, as seen in table 1 that the incidences stated of glaucoma with glaucomatous field loss in the series from ophthalmic practices ranged from 0·6 to 2·5 per cent.

The three youngest patients were 48, 57 and 59 years of age respectively while the remaining were over 65.

12 newly diagnosed cases of glaucoma at an advanced stage within the period from October 1 1960 to February 28 1962 corresponds to 8·4 patients annually.

By way of comparison it may be stated that prior to the introduction of routine tonometry 7·8 fresh glaucoma cases were recorded annually over a five year period on the Island of Falster.

Regarding the relation between screening tension and diagnosing of glaucoma it appeared that in three cases despite screening tensions below 20 mm Hg (in one eye) a diagnosis of glaucoma was subsequently established of this eye. In one case the eye even presented both cupping of the disc and fairly extensive visual field defects.

Choice of 21 mm Hg as the screening level would have reduced the number of patients for further examination from 169 to 123. In other words only 73 per cent of the original number of patients would have been registered for further examination. The number of patients with diagnosed glaucoma would

Table 11

Age and sex distribution of 12 patients who had a glaucomatous optic disc or fairly extensive visual field defects

	35-44	45-54	55-64	65-74	75-84	Total
males	-	-	2	4	2	8
females	-	1	-	2	1	4
Total	-	1	2	6	3	12

examinations Linner & Stromberg (1964) and Armaly (1969) hold that no definite conclusions can be drawn from the results of tonography whereas Leydhecker (1968 b) claims to have demonstrated a relationship in this respect

The problems relating to employment of the priscol test and the water provocative test have been discussed in two previous papers (Norskov 1966 1967 a) These studies showed that of the two tests when employed on the same patients and with limits of a positive issue fixed at 11 mm Hg and 8 mm Hg respectively the priscol test would most frequently cause a pathological rise (41 and 22 per cent respectively) in agreement with Leydhecker's statements (1955) The patients included in the present investigation proved however to dislike the priscol test so much that the author on this account found the test to be unsuitable for ordinary clinical use

A tendency prevails towards increasing the demands on the provocative tests Thus for instance attention has been given to the question whether a graduation according to age of the limit of a pathological rise is required (Wesberry *et al* 1966 Ballin & Becker 1967) In the series under review 15 per cent of the positive results of the water provocative tests occurred in persons aged over 65

Classification of Patients with Ocular Hypertension in Glaucoma

Borderline Cases and Normals

Such a classification is rendered difficult by the disagreement regarding the definition of glaucoma without field loss

Further various screenings are somewhat difficult to evaluate because the information available concerning the glaucoma criteria is not sufficiently accurate to allow of an estimate of the basis on which the stated incidence of glaucoma has been attained to

The glaucoma criteria chosen in the present investigation are in fair agreement with those stated in other Scandinavian papers dealing with routine tonometry studies (Corydon Andersen 1958 Bertelsen *et al* 1965 Norskov 1967 b 1970 a Bjornsson 1967 Jensen 1968)

In the series under review the incidence of glaucoma was 4.0 per cent among patients aged over 35 In the other series from ophthalmic practices the incidences stated ranged from 1 to 5 per cent (table 1)

The incidence for males was 4.2 per cent and that for females 3.9 per cent These figures are in fair agreement with those given by Ascher (1962) - males 3.3 per cent and females 2.6 per cent and Bjornsson (1967) - males 5.0 per cent and females 4.7 per cent and with the usual statements of the distribution of simple glaucoma between males and females (Leydhecker 1960)

The incidence rises with increasing age even considerably so after the age

only 18 eyes (14 per cent) not less than three criteria were available to justify establishment of the diagnosis. In this connection we must however make allowance for the greatly varying frequency of accomplishment for the different methods of investigation.

The criterion most frequently present was that of pressure values recorded at 25 mm Hg or higher which occurred in 94 eyes.

In 58 patients such high values were a bilateral phenomenon while 17 patients had the glaucoma diagnosis established for one eye only. In 12 of these cases the other eye was characterized as a borderline case and in four as normal. One patient was one eyed.

A comparison of the incidence of closed angle glaucoma with that of simple glaucoma showed as might be expected a considerable predominance of the latter form, only two patients having displayed a gonioscopically closed angle.

Table 10 shows the age and sex distribution of the 75 patients. The total number of diagnosed glaucoma cases constituted 40 per cent of the original number of examined patients. The incidence was found to rise with increasing age. No cases occurred in the age group under 40 but the incidence rose from 1.4 per cent in the age group of 45-54 to 3.2 per cent in that of 55-64. The highest rise from 3.2 to 9.0 per cent was noticed from the age group of 55-64 to that of 65-74.

For males and females the diagnosed glaucoma cases constituted 4.2 and 3.9 per cent respectively. The highest rise in number for both males and females was seen from the age group of 55-64 to that of 65-74. Otherwise the distribution varied somewhat within the individual age groups.

Table 10

Age and sex distribution of 75 patients who had the glaucoma diagnosis established

	males		females		Total	
	number	%	number	%	number	%
35-44	2	1.6	2	0.80	4	1.1
45-54	2	0.92	6	1.6	8	1.4
55-64	4	3.0	9	3.3	13	3.2
65-74	11	11.3	17	8.0	28	9.0
75-84	8	8.8	12	12.4	20	10.6
≥ 85	1	(11.1)	1	(9.1)	2	(10.0)
Total	28	4.2	47	3.9	75	4.0

patients concerned really do attend. At the same time however one must take care not to render the patient apprehensive.

In the present study we proceeded by explaining to the patient that the tension in the eye was a little above normal and that on this account we advised control within 1-3 months. However by this procedure 30 per cent failed to appear. Other ophthalmologists have had difficulties of the same kind in their practices. Reed & Bendor Samuel (1957) and Bendor Samuel *et al* (1960) stated that 30 and 38 per cent respectively of their patients failed to attend.

The experience gained from the present investigation goes to show that the number of absentees can be reduced by proposing control after one month at most and preferably at a fixed date. Summoning by letter effected that 82 per cent of the absentees were examined later.

In planning the further examinations we must aim at a reasonable balance between the examinations judged to be necessary for taking a decision on the suspicion of glaucoma raised by routine tonometry and the examinations that are practicable in consideration of work load economy and the patient's psyche.

In arranging the further examinations we originally aimed at a procedure fitting in with the conditions available to the ophthalmologist with no support from an ophthalmic unit. The reasons why hospitalisation was nevertheless employed were partly a desire for rapid accomplishment of the examination in question and partly to render the examination more convenient to the patients living far away from the ophthalmologist.

Many of the patients were however unwilling to accept admission to hospital. As many as one fourth of the patients whose examination had been arranged refused admission.

On the other hand it was often difficult to make the patients who had been through the entire series of examinations accept that the results achieved afforded no basis for any treatment of their eyes.

If however the ophthalmic medical practitioner is to carry through further examinations on the lines stated in the present paper which by no means can be characterized as ideal this cannot be done without a radical change of the usual working rhythm. The consultation hours will have to be prolonged in consequence of the many control pressure measurements and provocative tests and 24 hour pressure measurements cannot take place within the usual consultation hours.

The provocative tests play a prominent role in the diagnosis of glaucoma without field loss. However their use has the definite disadvantage that from a clinical aspect the tests afford no possibility of foretelling which patients are liable to future development of visual field defects.

Regarding tonography different views prevail on the basis of follow up

As shown in table 11 12 patients (eight males and four females) had glaucoma at a fairly advanced stage that is with a glaucomatous optic disc or more extensive visual field defects. These constituted 0.64 per cent of the 1882 subjected to routine tonometry the incidence being 1.2 per cent for males against only 0.33 per cent for females. By way of comparison it may be mentioned as seen in table 1 that the incidences stated of glaucoma with glaucomatous field loss in the series from ophthalmic practices ranged from 0.6 to 2.5 per cent.

The three youngest patients were 48, 57 and 59 years of age respectively while the remaining were over 60.

12 newly diagnosed cases of glaucoma at an advanced stage within the period from October 1, 1960 to February 28, 1962 corresponds to 8.4 patients annually.

By way of comparison it may be stated that prior to the introduction of routine tonometry 78 fresh glaucoma cases were recorded annually over a five year period on the Island of Falster.

Regarding the relation between screening tension and diagnosing of glaucoma, it appeared that in three cases despite screening tensions below 20 mm Hg (in one eye) a diagnosis of glaucoma was subsequently established of this eye. In one case the eye even presented both cupping of the disc and fairly extensive visual field defects.

Choice of 21 mm Hg as the screening level would have reduced the number of patients for further examination from 169 to 123. In other words only 73 per cent of the original number of patients would have been registered for further examination. The number of patients with diagnosed glaucoma would

Table 11
Age and sex distribution of 12 patients who had a glaucomatous optic disc or fairly extensive visual field defects

	45-49	50-54	55-59	60-64	65-69	70-74	Total
males	-	-	2	4	2	3	9
females	-	1	-	1	1	1	4
Total	-	1	2	5	3	4	12

glaucoma per October 1 1960 prior to the introduction of routine tonometry was 0.30 per cent (61 patients) for persons aged over 40. The prevalence of simple glaucoma was 0.23 per cent (48 patients).

It is shown in table 12 that Hurland & Taub (1951) and Corydon Andersen (1958), in similar reports from geographically well defined territories found a prevalence of primary glaucoma in the same age group of 0.34 per cent and 0.45 per cent respectively.

For the sake of comparison the table also gives the prevalence of primary glaucoma with associated visual field defects disclosed on two population examinations. Stromberg (1962) examined 80 per cent of the inhabitants aged

Table 12
Prevalence of primary glaucoma in geographically well defined population groups

A	population group	number of inhabitants	PREVALENCE	
			primary glaucoma	simple glaucoma
Hurland & Taub (1951)	Rochester Minnesota USA	9521 (≥ 40 yrs) (31.12.1954)	0.34%	0.27%
Corydon Andersen (1958)	Horsens Denmark	11 634 (≥ 45 yrs) (31.12.1957)	0.45%	-
Nørskov (1960)	Falster Denmark	20 601 (≥ 40 yrs) (1.10.1960)	0.30%	0.25%
B				
Stromberg (1962)	Skovde Sweden	9245 (≥ 40 yrs)	0.35%	-
Hollings & Gaham (1965)	Rhondda Valley Wales	4608 (40-75 yrs)	0.51%	0.43%

A calculated from occurrence of clinically recognized glaucoma in the territory concerned

B population studies

at the same time have been reduced from 75 to 68. This means that 9 per cent of the original number of glaucoma cases would have failed to be recognized among which three with glaucomatous field loss.

With a screening level of 22 mm Hg only 89 patients or 53 per cent of the original number would have been subjected to further examination. At the same time however the glaucoma diagnosis would not have been made in 12 cases or 16 per cent of the original number of glaucoma cases. Four of these patients had glaucoma with field loss.

Finally by altering the screening level to 25 mm Hg the number of patients for further examination would be reduced from 169 to 47. This means that only 28 per cent of the original number would have been further examined. At the same time the number of diagnosed glaucoma cases would have been reduced from 75 to 40. In other words the missed glaucoma cases would have constituted 47 per cent of the original number diagnosed. Seven of these patients had glaucoma with field loss.

Another possibility is that of graduating the screening value according to the patient's age. If thus the screening level for patients between the ages of 35 and 64 had been altered to 22 mm Hg the number of patients to be subjected to further examination would have been reduced from 15 to 29. Accordingly no more than 39 per cent of the original number from this age group would be referable to further examination. At the same time the number of patients with diagnosed glaucoma would have been reduced from 25 to 19. In other words 24 per cent of the original number of newly diagnosed glaucoma cases would have been missed including two with glaucomatous field loss.

If 25 mm Hg had been chosen as the screening level for the age group over 65 the number of patients for further examination would have been reduced from 94 to 33 or no more than 35 per cent of the original number would have been referred to further examination. At the same time the number of diagnosed glaucoma cases would have been reduced from 50 to 28. Thus 44 per cent of the original number of newly diagnosed glaucoma cases would have been missed including three with glaucomatous field loss.

In tracing glaucoma one should further according to Becker & Shaffer (1965) utilize the anamnestic data available knowing that a relationship exists between glaucoma and central vein thrombosis, glaucoma and diabetes, glaucoma and high myopia, glaucoma and thyroid dysfunction as well as glaucoma and pseudo exfoliation.

Among the patients with screening values above 20 mm Hg twelve had diabetes, eight central vein thrombosis, three high myopia, one thyroid dysfunction and one pseudo exfoliation. A diagnosis of glaucoma was established in six of the patients with diabetes, seven with central vein thrombosis, two with high myopia and one with pseudo exfoliation.

of 60. Among the patients ranging in age from 60 to 74 glaucoma was in fact diagnosed in every 11th of the patients seen. Ascher (1962) found the incidence to be 6.7 per cent among patients aged over 60. Björnsson states 6.6 and 10 per cent for the age groups of 60-69 and 70-79 respectively.

The borderline cases constitute an ill defined group of patients within the pressure range of 20-24 mm Hg. The work with which the ophthalmologist going in for routine tonometry is burdened depends greatly on the size of this group which also determines the number of patients to be troubled with continual control.

Disagreement prevails regarding the chance that glaucoma with field loss may develop from this group of borderline cases. Various ophthalmologists who have undertaken screenings take the chance to be so great that they have included the borderline cases in their calculations of the glaucoma incidence among others (Brav & Kirber 1951, Corydon Andersen 1958, Packer *et al* 1959, Dunbar & Goldberg 1960, Linner & Stromberg (1964, 1967) on the other hand state that persons with a moderate ocular hypertension rarely develop glaucoma with field loss.

Adoption of the view that borderline cases have such a great chance of developing into glaucoma with field loss would with the criteria chosen in the present study have involved continued control of a number of patients of the same order as those with manifest glaucoma, i.e. 4.1 per cent of the 1882 patients subjected to routine tonometry. The incidence is however lower - 0.4 to 1.4 per cent - in the series from ophthalmic practices in which this has been calculated for the borderline cases (table 1).

The number of borderline cases depends in some measure on the extent of further examinations, the criteria for establishing the glaucoma diagnosis and also on the criteria chosen for normality. In the present study it was required that all the control examinations gave values within the normal range including tension measurements below 20 mm Hg.

If thus in the present investigation a value of 21 mm Hg had been regarded as within the normal range the incidence of borderline cases would have fallen from 4.1 to 2.6 per cent.

Thus in attempting to form an estimate of the usefulness of routine tonometry it is highly inconvenient that such great uncertainty also prevails regarding the differentiation between borderline cases and normals.

Relation between Glaucoma with and without Glaucomatous Field Loss

Our knowledge concerning the prevalence of glaucoma with field loss is very deficient despite comprehensive statistics from ophthalmic clinics (Leydhecker 1960) and results reported of a considerable number of screenings.

On the Island of Falster the prevalence of clinically recognized primary

Normals

This group comprised patients for whom the total number of control examinations of both eyes gave results within the normal range including control pressure measurements below 20 mm Hg

16 patients (15 males and 1 female) were included in this group. This means that 9.5 per cent of the 169 screening positive patients subsequently could be declared normal. The result of the screening test must thus in these cases be characterized as false positive.

Borderline Cases

This group comprised the cases in which the examinations carried out and the criteria laid down for establishing the glaucoma diagnosis or characterizing the condition as normal (see above) afforded no basis for confirming or refuting a diagnosis of glaucoma.

A total of 18 patients (141 eyes) were included in this group constituting 4.1 per cent of the original number examined: 23 males (3.4 per cent) and 55 females (4.6 per cent).

In 65 cases this phenomenon was bilateral while in 13 one eye was normal. Two patients of this group were one-eyed.

As stated previously 12 patients with one eye characterized as a borderline case and the other as glaucomatous were included in the glaucoma group.

The demand for control tension values below 20 mm Hg as a criterion of normality contributed particularly to the considerable number of borderline cases. By altering this demand to below 21 mm Hg the number of borderline cases would have been greatly reduced from 78 to 49 or from 4.1 to 2.6 per cent of the original number of examined patients.

Discussion

A direct comparison of the series mentioned in table 1 originating from other ophthalmic practices and that constituting the basis of the present investigation has been rendered difficult by differences regarding a number of the factors influencing the results achieved. These factors are such as differences in composition of the groups of patients examined from the individual practice, the screening level chosen, the extent of further examinations and the glaucoma criteria employed.

In the study under review the practice series was preserved as an entity similarly as were most of the series included in table 1. The only patients ruled out were those with previously recognized glaucoma and patients with eyes in a state of acute ocular inflammation.

After further examinations including provocative tests the glaucoma diagnosis was established in 4.0 per cent (75 patients). No more than 12 of these patients (0.64 per cent) had glaucoma with a fairly extensive field loss. Only two patients had closed angle glaucoma.

The borderline cases constituted 4.1 per cent (18 patients) 16 patients (9.5 per cent of those subjected to further examinations) were characterized as normal; all the control examinations having revealed normal conditions including tension values below 20 mm Hg.

Under the impression of the enormous work with which the ophthalmologist going in for routine tonometry is burdened suggestions are advanced for modifications of the screening procedure. In addition mention is made of other possibilities of disclosing glaucoma without field loss.

Furthermore the difficulties are stated of distributing patients with ocular hypertension in the groups of glaucoma cases, borderline cases and normals. These difficulties seem to give a reasonable explanation of the considerable difference between the prevalence of clinically recognized glaucoma on the Island of Falster (0.30 per cent for persons aged over 40) and the great number of newly diagnosed glaucoma cases found during the present investigation by examining a group of patients constituting 9 per cent of the population of Falster aged over 40.

References

- Andersen O. Corydon. Die häufigkeit des Glaukoms. *Acta Ophthal* 1938 36 612-650.
- Andersen O. Corydon. Bemerkungen zu den Aussetzungen Lautersteins. *Klin. Mbl. Augenheilk.* 1964 145 65-71.
- Armaly M. F. The Des Moines population study of glaucoma. *Invest. Ophthal* 1962 1 6 3-6.
- Armaly M. F. On the distribution of applanation pressure. *Arch. Ophthal* 1963 3 11-18.
- Armaly M. F. Ocular pressure and visual fields. *Arch. Ophthal* 1969 87 95-100.
- Atchey H. W. Die Suche nach undiagnostizierten Glaukomfällen. *Klin. Mbl. Augenheilk.* 1967 140 516-524.
- Althaus E. & H. Harms. Papillenveränderung und Gesichtsfeldstörung beim Glaukom. *Ophthalmologica* 1960 149 219-235.
- Bollin A. & B. Becker. Provocative testing for primary open angle glaucoma in senior citizens. *Invest. Ophthal* 1967 6 176-181.
- Becker B. & R. V. Shaffer. *Diagnosis and therapy of the glaucomas*. 2 ed. Saint Louis 1964 p. 53 145 & 184-185.
- Bendix Saund J. E. L. W. May & H. Reed. Routine tonometry in 5000 patients for detection of early glaucoma. *Brit. med. J.* 1960 1 355-355.
- Bertelsen T. W. Daanger A. Kolstad L. Worsching & H. Aasved. Måling av det intraokulære trykk (Schwitz) og spaltelampeundersøkelse av personalet i en storbedrift. *Tidsskr. norske Lægeforen* 1965 85 449-453.

Table 2

A comparison of the frequency of positive DT in blind children at Dalen State School for the Blind and in a control group

Age in years	Group	No of sera	No of positive	Per cent of positive	Probability ¹
7-10	Dalen	30	14	47	$P < 0.001$
	Control	83	11	13	
11-14	Dalen	29	15	52	$P < 0.001$
	Control	117	20	17	

¹ χ^2 test

late DT titres and diagnosis. There are obvious difficulties in diagnosing ocular toxoplasmosis in blind children showing a positive DT. The prevalence of past or persistent toxoplasmosis in the general population reduces the diagnostic value of DT in older children. The problems of causal relationships might be elucidated by further investigations, especially in younger age groups.

Summary

The frequency of positive DT in blind children at the Dalen State School for the Blind, Norway, has been studied. This frequency was significantly higher than in a control group.

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References

- Fa. J. P. *Surv. Ophthalmol.* 6: 3955, 1961.
- Conlath J. A. *Int. J. & Medvet. T. Acta ophthalmol.* 40: 181-185, 1960.
- Hogan M. J. *Surv. Ophthalmol.* 6: 955-94, 1961.

- Midtvedt T* Acta Paed scand 54 81 82 1965
- Perkins E S* Uveitis and toxoplasmosis J C A Churchill Ltd London 1961
- Ramseil T G & Gamero B A* Brit J Ophthalmol 51 282 288 1967
- Rieger H* Die Augenveränderungen bei der Toxoplasmosis acquisita in Toxoplasmosis Georg Thieme Verlag Stuttgart 1962

over 40 in Skövde Sweden while Hollows & Graham (1966) examined 91.9 per cent of the persons aged between 40 and 75 living in Rhondda Valley Wales

As seen in table 12 there is fair agreement between the prevalence of clinically recognized primary glaucoma and the prevalence of primary glaucoma with visual field defects recorded in relation to the population examinations

It is therefore surprising that on Falster routine tonometry in an ophthalmic practice of a group of patients constituting 9 per cent of the population aged over 40 revealed in the course of 18 months 75 fresh cases of glaucoma on the basis of the chosen criteria which are those commonly employed at routine tonometry in the Scandinavian countries

The most reasonable explanation of this problem is that with the diagnostic aids available at present we have only a slight possibility of distinguishing between ocular hypertension and glaucoma which later will develop visual field defects

The final answer to the question of the value of routine tonometry can however only be given on the basis of follow up examinations carried through in relation to glaucoma screening. In a future paper an account will be given of a recently concluded five year follow up carried out in continuation of the present investigation

Summary

The present study is based on routine tonometry carried out on 1882 patients aged over 35 who consulted the only ophthalmologist on the Island of Falster (93 per cent of the number attending)

Patients with previously recognized glaucoma and patients with acute ocular inflammatory states were ruled out

169 patients (9.0 per cent) had an applanation value recorded of 20 mm Hg or higher

Presence of one or more of the following criteria was required to establish the diagnosis

- 1 Distinct marginal cupping of the optic disc
- 2 Reproducible glaucomatous visual field defects
- 3 Pressure values measured ≥ 25 mm Hg
- 4 Water provocative test ≥ 8 mm Hg
- 5 Priscot provocative test ≥ 11 mm Hg
- 6 Mydriasis test ≥ 8 mm Hg
- 7 Dark room test ≥ 10 mm Hg

Table 3

Comparison of the pressure level on primary outpatient control examination with that on follow up examination after five years (136 eyes of 68 untreated patients)

	follow up examination			
	< 20 mm Hg	20-21 mm Hg	22-24 mm Hg	≥ 25 mm Hg
primary out patient control examination				
< 20 mm Hg	37	21	7	1
20-21 mm Hg	5	22	16	4
22-24 mm Hg	2	5	4	5
≥ 25 mm Hg	1	1	1	4

author in a previous study (1970a) This indicates that the intra ocular pressure cannot be taken as a fixed value but will undergo variations

Ophthalmoscopy 220 eyes (110 patients) were to be subjected to ophthalmoscopy which however could not be carried through for six eyes

Ten eyes were found to have a glaucomatous optic disc in agreement with the ophthalmoscopic finding on the primary screening

Out of seven eyes whose discs had originally been characterized as glaucoma suspicious four had developed a glaucomatous disc while the conditions remained unchanged in the remaining three eyes

Of the 197 eyes with discs originally characterized as normal 192 had remained unchanged while in three a glaucomatous disc had developed and in two a disc suspicious of glaucoma

Visual field measurements 101 patients had the visual fields measured at the follow up An estimation was impossible in the cases of nine patients owing to failing co operation or to presence of cataract or senile macular degeneration

The primary screening revealed visual field defects in 15 patients (22 eyes) In 11 patients (16 eyes) the defects were at the initial stage while in four (six eyes) they were at a more advanced stage

In six of the patients with beginning visual field defects (eight eyes) who had baring of the blind spot recorded at the primary screening despite normal discs the visual field defects were no longer visible on the follow up examination This is the more surprising because a pressure level below 20 mm Hg had been obtained neither with nor without treatment This observation stresses the doubtful value of considering baring of the blind spot as an early sign of glau

- Jersey J W Binocular disparity in normal eyes Eye Ear Nose Thr Monthly 1962 41 45-46
- Katausko M The diurnal variations of ocular tension in glaucoma Acta Ophthal suppl 18 kbh 1964 ■ 18 44 & 111-114
- Kurland L T & R C Taub The frequency of glaucoma in a small urban community Amer J Ophthal 1957 43 539-544
- Lauterstein M Bemerkung zum referat Leydhecker klin Mbl Augenheilk. 1960 13: 494-495
- Lauterstein M Einiges über das problem des fruhstadiums und der fruhdiagnose beim glaucoma simplex in der taglich n augenärztlichen praxis klin Mbl Augenheilk 1961 139 610-674
- Lauterstein M Zur fruhdiagnose des glaukoms in der augenärztlichen praxis klin Mbl Augenheilk. 1967 141 915-973
- Lauterstein M Über den diagnostisch prophylaktischen wert der obligatorischen tonometrie methode und der methode der selbstkontrolle beim glaucoma simplex und einige angrenzende probleme klin Mbl Augenheilk 1963 143 111-116
- Leydhecker W Provocative tests in glaucoma In S Duke Elder ed Glaucoma Oxford 1955 ■ 205-225
- Leydhecker W & Akizama Ch Meinke H C Neumann & G Schafhausen Die fehlergrösse der messung mit dem geeichten Schiötz tonometer am lebenden menschenauge klin Mbl Augenheilk 1958 13 855-860
- Leydhecker W Zur verbreitung des glaucoma simplex in der scheinbar gesunden augenärztlich nicht behandelten bevölkerung Documenta Ophthal 1959 13 359-380
- Leydhecker W Glaukom - ein handbuch Berlin 1960 p 31-34 57 151 & 340
- Leydhecker W Die anamnese bei glaucoma simplex klin. Mbl Augenheilk 1963 a 153 319-332
- Leydhecker W Wert und unwert der tonographie klin Mbl Augenheilk. 1963 b 153 857-860
- Linner E & U Stromberg The course of untreated ocular hypertension Acta Ophthal 1964 47 836-848
- Linner E & U Stromberg Ocular hypertension - a five year study of the total population in a Swedish town Skovde In Glaucoma symposium Tutzing Castle Basel 1967 ■ 187-194
- Nørskov A Priscot provocative test Acta Ophthal 1966 44 528-536
- Nørskov A The water provocative test Acta Ophthal 1967 a 45 57-67
- Nørskov A Routine tonometry for detection of glaucoma in inpatients with a five year follow up Acta Ophthal 1967 b 45 536-545
- Nørskov A Glaucoma screening - 1 Critical evaluation based on routine tonometry among members of the Volunteer Donor Corps of the Island of Falster (Denmark) Acta Ophthal 1968 48 401-417
- Nørskov A Glaucoma screening - 2 A five year follow up carried through in relation to a glaucoma screening among members of the Volunteer Donor Corps of the Island of Falster (Denmark) Acta Ophthal 1968 b 48 418-433
- Ourgaud A G & R Etienne L'exploration fonctionnelle de l'oeil glaucomateux vol 1 Paris 1961 p 7-14 67 & 92
- Packer H A A Deutsch Ph M Leuns C D Oglesby & A C Cheirj Study of the frequency and distribution of glaucoma JAMA 1959 171 1090-1093
- Phelp C B The incidence of glaucoma J Iowa St med Soc 1949 39 519-520

coma as claimed by various writers (Aulhorn & Harms 1967 Drance 1961 Goldmann 1967 Armafy 1969)

In five patients (eight eyes) the primary screening had revealed not only beginning visual field defects but also a glaucomatous or glaucoma suspicious optic disc. These patients were all under treatment. In four eyes the follow up examination showed progression of the visual field defects while in the four others the conditions had remained unaltered.

Of the six eyes (four patients) with primarily recorded fairly advanced visual field defects, three (two patients) showed progression of the visual field defects despite treatment and a pressure level of 20-21 mm Hg while in the other three eyes (two patients) the conditions had remained unaltered.

Out of 86 patients followed up who originally had normal discs and visual fields two (two eyes) developed visual field defects during the observation period.

An over all assessment of the course during the observation period based on ophthalmoscopy and visual field measurement gave progression of the glaucoma in ten (14 eyes) of the 110 patients followed up. Seven patients ranged in age from 59 to 72 at the time of the screening. The youngest patient was 57 and the oldest 81.

Regulation of the tension to below 20 mm Hg within the observation period was obtained in two eyes only while in nine eyes a level between 20 and 24 mm Hg was recorded and finally in three eyes 25 mm Hg or higher.

In four (seven eyes) of the ten patients showing progression there was progression of existing visual field defects or development of optic disc changes observed by ophthalmoscopy. Two patients (three eyes) had both glaucoma and central vein thrombosis and a man aged 57 presented closed angle glaucoma with associated glaucomatous field loss despite surgical treatment. Of the patients with originally normal conditions only three (three eyes) developed glaucomatous field loss. Their case histories will be briefly reported.

Case reports 1 (case 25/61 67) A man aged 63 with a screening tension of 26 mm Hg of both eyes. Ophthalmoscopy (including retinal photo) and visual field measurements showed normal conditions. All the control pressure values measured were 25 mm Hg or higher. Water provocative test released a rise from 21 mm Hg to 31 mm Hg in the right eye but no pathological rise in the left. The pilocarpin provocative test was negative in both eyes. Treatment was instituted with a resulting pressure level of 20-21 mm Hg of both eyes within the observation period. The follow up examination disclosed a definitely glaucomatous optic disc in the right eye but unchanged normal conditions in the left. Visual field measurement had to be given up owing to failing co-operation. Conclusion: development of glaucoma with field loss in the right eye.

2 (case 141/61 67) A woman aged 71 with a screening tension of 27 mm Hg of the right eye and 18 mm Hg of the left. In the right eye ophthalmoscopy (including retinal photo) and visual field measurement showed normal conditions. Several control pressure measurements gave values of 25 mm Hg or higher. Water provocative test re-

- Bjornsson G* The primary glaucoma in Iceland Thesis Acta Ophthal suppl 91 Kbh 1967 p 44 65-83 & 85
- Blaxter P L* Contribution to final discussion In L B Hunt ed Glaucoma London 1966 p 125
- Brav S S & H Küber* Mass screening for glaucoma JAMA 1951 147 1127-1128
- Bruens E* Zur fruhdiagnose des glaukoms in der augenärztlichen praxis Klin Mbl Augenheilk 1961 138 710-711
- Colenbrander M C* Measurement of the excavation Ophthalmologica 1960 139 491-493
- Davanger M* The difference in ocular pressure in the two eyes of the same person Acta Ophthal 1965 43 299-313
- Drance S M* The significance of the diurnal phasic variation of intraocular pressure in normal and glaucomatous eyes Arch Ophthal 1960 64 494-501
- Duke Elder S* System of Ophthalmology vol 7 The Foundations of Ophthalmology London 1962 p 212
- Dunbar J C & M C Goldberg* Second glaucoma survey of Allegheny county and environs Penn med J 1960 63 1802-1806
- Ehlers H* Den tidlige glaukomdiagnose Ugeskr Laeg 1960 122 1186-1188
- Fortier J P* Le glaucome probleme de santé publique Un med Can 1958 81 770-773
- Fronimopoulos J H Cofinas & N Lambrou* Die passive entdeckung des fruhstadiums des glaucoma simplex Klin Mbl Augenheilk 1965 46 416-419
- Gahn M A* The mydriasis provocative test Arch Ophthal 1961 66 353-355
- Gassler H* Über die häufigkeit von glaukomkranken unter neu aufgenommenen patienten der augenarztsprechstunde Klin Mbl Augenheilk 1965 146 362-367
- Goedbloed J J Schappert Kimmijser P C Donders H E Henkes J E A v d Heuvel B L Hocksema G A Jonkers J Obruik & N M J Schweitzer* Frequency distribution of intraocular pressure in the Netherlands Ophthalmologica 1961 141 481-488
- Goldmann H* Klinische methoden der untersuchung des intraokularen druckes und der abflussverhältnisse beim primären glaukom Ophthalmologica 1960 139 214-258
- Gorin G & A Posner* Slit lamp gonioscopy Baltimore 1957 p 60
- Graham P A & F C Hollows* A critical review of methods of detecting glaucoma In L B Hunt ed Glaucoma London 1966 p 103-115
- Hager H* Die behandlung des glaukoms mit miotika Bucherei des augenarztes 1958 29 p 14-18 & 27-28
- Harrington D O* The visual fields Saint Louis 1964 p 190
- Harris L S* Cycloplegic induced intraocular pressure elevations Arch Ophthal 1968 89 242-246
- Hildreth H R & B Becker* Routine tonometry Amer J Ophthal 1957 43 21-23
- Hollows F C & P A Graham* The Ferndale glaucoma survey In L B Hunt ed Glaucoma London 1966 p 24-44
- Holm E* Contribution to discussion on H Skydsgård Glaukomprofylakse Ugeskr Laeg 1960 122 1212-1215
- Holmes W H* Glaucoma in the central and south Pacific Amer J Ophthal 1961 51 253-261
- Hunt L B* ed Glaucoma London 1966
- Jensen J Bruun* Glaucoma screening with Schiøtz tonometer and tension indicator of applanation type Acta Ophthal 1968 46 638-642

leased a rise from 26 mm Hg to 34 mm Hg. No priscol provocative test was made. The condition of the left eye could not be assessed owing to cataract. All the control pressure values measured were below 20 mm Hg and the water provocative test gave a negative result. Treatment was instituted of the right eye. The pressure level was 95 mm Hg or higher during the observation period. In the left eye the intra ocular pressure remained below 20 mm Hg without treatment. The follow up examination showed in the right eye a definitely glaucomatous disc and visual field measurement revealed an arcuate scotoma superiorly with peripheral break through and defects in the upper nasal quadrant. In the left eye the condition was still impossible to assess owing to cataract. Conclusion: development of glaucoma with field loss of the right eye.

3. A woman aged 70 with screening tensions of 19 mm Hg (right eye) and 21 mm Hg (left eye). Ophthalmoscopy and visual field measurement showed normal conditions. The water provocative test released a rise from 19 mm Hg to 24 mm Hg in the right eye and from 21 mm Hg to 27 mm Hg in the left eye. No priscol provocative test was made. Control pressure measurements gave 20-21 mm Hg. Treatment was instituted after two years. The pressure level was 20-21 mm Hg during the observation period. On the follow up examination both discs were characterized as glaucoma suspicious. Visual field measurement revealed arcuate scotoma superiorly with no peripheral break through in the right eye and a normal visual field in the left. Conclusion: development of glaucoma with field loss of the right eye.

Provocative tests. An evaluation on the basis of the present investigation of the chances the provocative tests may have of prognosticating the further course must in any case be accepted with a certain reservation but is in particular interfered with by possible alterations caused by the therapy instituted.

Considering with this reservation the patients who developed glaucomatous field loss despite treatment and who had a water provocative test carried through we found a pathological rise (≥ 8 mm Hg) in no more than three out of 11 eyes.

Another question suggesting itself in this connection is whether the result of the water provocative test may predict a rise of the tension to a pathological level - in this study set arbitrarily at 25 mm Hg. Among the patients characterized as *borderline cases* and *patients with untreated glaucoma* such a situation without glaucomatous field loss was present in seven (11 eyes) and five (1 eyes) respectively. Only three out of these 18 eyes showed a pathological rise.

Estimated on the basis of these findings the water provocative test seemed to give no indication of the further course neither for the patients presenting an additional field loss at the follow up nor for the patients who developed a pressure level of 25 mm Hg or higher during the observation period.

The priscol provocative test could not be assessed on the same lines owing to the small number of tests available.

The course among the 110 followed up patients considered in relation to classification in glaucoma cases, borderline cases and normals. The object of this assessment was to get an impression of the extent to which the original classification could be maintained after five years. In this connection we must bear in

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ROUTINE TONOMETRY IN OPHTHALMIC PRACTICE

II Five Year Follow Up

BY

KNUD NØRSKOV

The desire for an intensification of the glaucoma prophylactic work by means of routine tonometry is based primarily on the fact that using the traditional form of glaucoma tracing the disease has in fact been found to be among the three most frequent causes of blindness (Rapp epidem demogr 1966 Nørskov 1968)

Furthermore it is a common clinical impression that the prognosis of simple glaucoma traced before field loss has set in is considerably more favourable than that of glaucoma at an advanced stage. However only few comprehensive investigations all retrospective are available in support of this impression as mentioned by Leydhecker 1960a, Dake 1967 and Leopold 1967 among others.

Moreover employment of routine tonometry in the glaucoma prophylactic work requires that it is possible by tonometry to single out the persons who later will develop visual field defects in accordance with the hypothesis advanced by Leydhecker (1959) and Goldmann (1959) that the ocular hypertension precedes the visual field defects by 15-18 years.

However in spite of a very considerable number of glaucoma screenings carried through only few reports on follow up examinations are available by which to assess the further course in cases traced by routine tonometry.

mind however that a possibly modified characterisation was based solely on ophthalmoscopic and visual field alterations and on alteration of the pressure level the follow up examination having not included provocative tests

In conformity with the previously chosen criteria a pressure level below 20 mm Hg was characterized as normal a pressure level of 20-24 mm Hg as a borderline range and 25 mm Hg or higher as an arbitrarily chosen pathological level

The classification of the 110 patients followed up is shown in table 1 50 patients had glaucoma of one or both eyes 48 patients were characterized as borderline cases and 12 patients as normal

Glaucoma The age and sex distribution is seen in table 1 Of the 50 patients 13 had remained untreated while 37 (72 eyes) had received antiglaucomatous drug treatment in seven cases (12 eyes) supplemented by surgical intervention

Table 4 renders pressure levels for the 37 patients (72 eyes) subjected to treatment. It is seen that a regulation of the tension to below 20 mm Hg was obtained in no more than 14 eyes

In 29 patients no glaucoma provoked alteration was noticed of central visual acuity ophthalmoscopic findings or visual field

Eight patients (11 eyes) presented progression of the glaucoma Two of these showed central vein thrombosis as well of one eye while in two other cases (two eyes) the disease had developed from previously normal conditions (cases 1 and 2)

The other four patients (six eyes) showed progression of existing visual field defects

In six patients improvement of the state was observed In five of these (six eyes) as stated above a previously noticed haring of the blind spot was not re

Table 4
Pressure level during the observation period in 50 patients (98 eyes) characterized as glaucoma cases

pressure level	without treatment	with treatment	Total
< 20 mm Hg	6	14	20
20-24 mm Hg	3	20	23
25-29 mm Hg	6	29	35
≥ 30 mm Hg	11	9	20
Total	26	72	98

- Pietruschka G *Klinische untersuchungen zur frage der atiology des primaren glaukoms* Halle 1959 p 112
- Pollack I P The challenge of glaucoma screening *Surv Ophthal* 1968 13 4-9
- Porter G LeRoy Incidence and detection of glaucoma by routine tonometry *Trans amer acad Ophthal Otolaryng* 1958 62 51-61
- Posner A & W G Fogland Mass screening for glaucoma a critical review of methods now in use *Eye Ear Nose Thr Monthly* 1964 43 53-61
- Reed H & J E L Bendor Samuel The detection of glaucoma before evidence of visual impairment *Trans ophthal Soc UK* 1957 77 319-391
- Schmidt Klin Mbl Augenheilk 1959 135 859-860
- Schmidt Th Zur fruhdiagnose und uberwachung des einfachen glaukoms *Ophthal mologica* 1960 139 265-270
- Segal P & J Skwierzyńska Mass screening of adults for glaucoma *Ophthalmolo gica* 1967 153 336-348
- Shaffer R N Gonioscopy ophthalmoscopy and perimetry *Trans Amer Acad Oph thal Otolaryng* 1960 64 112-127
- Shapiro I S & H H Levine Integrating glaucoma detection into group medical practice *Amer J Publ Hlth* 1965 55 1638-1642
- Shutt H A R T A S Boyd & A B Salter The relationship of visual fields optic disc appearances and age in non glaucomatous and glaucomatous eyes *Canad J Ophthal* 1967 2 83-90
- Sloan M W The importance of early diagnosis in narrow angle glaucoma *Henry Ford Hosp Bull* 1957 5 245-249
- Sloan M W Glaucoma control *Amer J Ophthal* 1959 47 641-649
- Snydercler D The normal optic disc *Amer J Ophthal* 1964 58 958-964
- Stromberg U Ocular hypertension Thesis *Acta Ophthal suppl* 69 kbh 1962
- Traquair H M An introduction to clinical perimetry London 1938 p 132-133
- Tuominen E Therapeutic results in primary glaucoma *Acta Ophthal suppl* 67 kbh 1961 p 29
- Vaughan D G R V Shaffer T Asbury S R Mettler W L Ridgway & R A Lotspeich Glaucoma detection in private practice and hospital *Sight sav Rev* 1957 27 145-148
- Waardenburg P J A Francechetti & D Klein Genetics and Ophthalmology Assen 1961 p 610
- Walker W M Contribution to final discussion In L B Hunt ed *Glaucoma* London 1966 p 121
- Walser E Bemerkungen zur glaukomdiagnostik unter besonderer berucksichtigung der instrumentellen und palpatorischen augendruckprufung *Klin Mbl Augenheilk* 1965 147 404-409
- Webb J M R Hiatt A Deutsch & Ph M Lewis Analysis of false positive borderline diagnosis in a glaucoma detection program *Amer J Ophthal* 1966 61 859-866
- Westerlund E Clinical and genetic studies on the primary glaucoma diseases Thesis kbh 1947 p 149
- Wright J E The Bedford glaucoma survey In L B Hunt ed *Glaucoma* London 1966 p 12-17
- Yusupov A Yu & L I Sumatkhina Glaucoma among the organized population of the city of Samarkand *Vestn Ostal* 1963/5 53-55

producible and in one the extent of the visual field defects became reduced after a cataract operation

Table 4 also shows the pressure levels in the 13 untreated cases. It is seen that in two thirds of the cases (17 eyes) the pressure level was 22 mm Hg or higher. In spite of this none of the untreated glaucoma patients displayed any glaucoma provoked alterations of visual field and ophthalmoscopic findings.

Of the 12 patients with fairly advanced glaucoma at the time of the primary screening, seven (10 eyes) were followed up. Additional progression was recorded in half of these eyes despite treatment and a pressure level of 20-24 mm Hg while in the other half the conditions had remained unchanged. In two of the latter eyes the pressure level was above 25 mm Hg. All in all these findings stress the bad prognosis for eyes presenting a rather extensive glaucomatous field loss.

Glaucoma according to the chosen criteria was unilaterally present in ten of the patients followed up. Six of these had both eyes treated. Only a single patient had developed visual field defects of the non glaucomatous eye.

Borderline cases The age and sex distribution of 48 patients is seen in table 1.

43 patients remained untreated during the observation period and visual field measurement and ophthalmoscopy revealed no glaucomatous changes in these cases. An altered characterisation in keeping with the stated criteria must therefore be based solely on the pressure values during the observation period.

It is shown in table 5 that during the observation period pressure levels below 20 mm Hg were recorded in 17 eyes without treatment but only in four patients in both eyes. In conformity with the criteria employed these latter borderline cases should be characterized as normal after the follow up.

Table 5 also shows that during the observation period pressure levels of 25 mm Hg or higher were recorded for four eyes (three patients). These eyes all

Table 5

Pressure level during the observation period in 48 patients (96 eyes) characterized as borderline cases

pressure level	without treatment	with treatment	Total
< 20 mm Hg	17	1	18
20-21 mm Hg	33	4	47
22-24 mm Hg	27	5	32
≥ 25 mm Hg	4	-	4
Total	86	10	96

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ROUTINE TONOMETRY IN OPHTHALMIC PRACTICE

II Five Year Follow Up

BY

KNUD NORSKOV

The desire for an intensification of the glaucoma prophylactic work by means of routine tonometry is based primarily on the fact that using the traditional form of glaucoma tracing the disease has in fact been found to be among the three most frequent causes of blindness (Rapp, *epidem. demogr.* 1966, Nørskov 1969).

Furthermore it is a common clinical impression that the prognosis of simple glaucoma traced before field loss has set in is considerably more favourable than that of glaucoma at an advanced stage. However only few comprehensive investigations, all retrospective, are available in support of this impression as mentioned by Leydhecker 1960a, Dake 1967 and Leopold 1967 among others.

Moreover employment of routine tonometry in the glaucoma prophylactic work requires that it is possible by tonometry to single out the persons who later will develop visual field defects in accordance with the hypothesis advanced by Leydhecker (1959) and Goldmann (1959) that the ocular hypertension precedes the visual field defects by 15-18 years.

However in spite of a very considerable number of glaucoma screenings carried through only few reports on follow up examinations are available by which to assess the further course in cases traced by routine tonometry.

presented a rise from 22–24 mm Hg to maximally 27 mm Hg. The three cases should accordingly be characterized as having changed from borderline cases to glaucoma cases but as stated without glaucomatous field loss.

Five patients had treatment instituted after a pressure level of 25 mm Hg or higher had been recorded within the observation period. It is seen in table 5 that despite treatment regulation of the tension to below 20 mm Hg was obtained in a single case only. One patient (case 3) with previously normal conditions had developed visual field defects while another with originally glaucoma suspicious discs had developed distinct marginal cupping of the optic discs where visual field measurement could not be carried through.

The over all result of the follow up examination of 48 patients primarily characterized as borderline cases was that for eight the characterisation had to be altered to glaucoma though only in two cases with glaucomatous field loss while four were to be characterized as normal.

Normals. Table 1 shows the age and sex distribution of 12 patients characterized as normal after further examinations. Neither visual field measurement nor ophthalmoscopy revealed any glaucoma provoked alterations and seven patients had unaltered pressure values below 20 mm Hg. Five patients had pressure values of 20–21 mm Hg recorded. These should therefore according to the chosen criteria be transferred from the group of normals to that of borderline cases. However the shifts of tension values are seen to have been small.

Assessment of the further course among the 110 patients followed up considered in relation to alterations of the screening level. In the endeavours to reduce by routine tonometry the number of patients referable to further examination we aimed on the primary screening at getting an impression of the relation between an alteration of the screening level and the number of missed glaucoma cases. We proceeded by raising the screening level to ≥ 21 , ≥ 22 and ≥ 25 mm Hg respectively together with a graduation according to age. Thus the screening level was altered to 22 mm Hg or higher for patients aged between 35 and 64 and to 25 mm Hg or higher for patients aged over 65. The stated alterations of the screening procedure effected as might be expected a reduction of the number of patients referable to further examination but at the expense of missed glaucoma cases judged from the criteria chosen (Nørskov 19 0b).

It will therefore be valuable to have the further course clarified for the patients missed owing to the respective alterations of the screening level to be able to estimate which alterations might be warranted.

A rise of the screening level to 21 mm Hg at the primary screening would have effected that 38 of the 110 patients followed up had not been suspected of glaucoma on routine tonometry. Four of these patients characterized as having glaucoma were treated without obtaining a pressure level below 20 mm Hg. None of the 38 patients developed visual field defects within the observation

The results of the follow up examinations carried out go to show that routine tonometry contributes towards intensifying the glaucoma tracing work (Leydhecker 1960b 1966) and at the same time that employment of tonometry is of limited value as an aid to singling out the persons who later will develop glaucoma with field loss (Linner & Stromberg 1964 1967, Becker & Morton 1966 Armaly 1969 Nørskov 1970a)

Investigations with a view to assessing the further course among normals have been undertaken by Armaly (1960 1962 1969) Linner & Stromberg (1967) and in previous studies by the author (Nørskov 1967, 1970a)

In the present paper the results will be reported of a five year follow up performed in relation to applanation tonometry carried out as a routine among patients in ophthalmic practice

The investigation comprised follow up examination and assessment of the course in the patients suspected of glaucoma after routine tonometry Further the investigation included assessment of the course based on information given by the only ophthalmologist of Falster regarding the patients who after applanation tonometry had been characterized as normal

Own Material

In a previous paper (Nørskov 1970b) the results are reported of routine tonometry among patients aged over 30 on the Island of Falster who consulted the only ophthalmologist of Falster within the period from October 1 1960 to February 28 1967

Among the 1882 patients subjected to applanation tonometry 169 (9.0 per cent) had an intra ocular pressure of 20 mm Hg or higher recorded

Establishment of the glaucoma diagnosis required presence of one or more of the following criteria 1 distinct marginal cupping of the optic disc 2 reproducible glaucomatous visual field defects 3 pressure values ≥ 20 mm Hg 4 rise ≥ 8 mm Hg in response to water provocative test 5 rise ≥ 11 mm Hg in response to prisol provocative test 6 rise ≥ 8 mm Hg in response to mydriasis test 7 rise ≥ 10 mm Hg in response to darkroom test

75 patients had the glaucoma diagnosis established in one or both eyes while 18 were characterized as borderline cases and 16 as normal

After the examination with a view to tracing glaucoma another ten patients were regarded as suspects despite a screening tension below 20 mm Hg However none of these later had the glaucoma diagnosis established

1703 patients were characterized as normal after routine tonometry

A five year follow up was carried through in November and December 1966 an out patient follow up examination having been arranged in the ophthalmic

producibile and in one the extent of the visual field defects became reduced after a cataract operation

Table 4 also shows the pressure levels in the 13 untreated cases. It is seen that in two thirds of the cases (17 eyes) the pressure level was 22 mm Hg or higher. In spite of this none of the untreated glaucoma patients displayed any glaucoma provoked alterations of visual field and ophthalmoscopic findings.

Of the 12 patients with fairly advanced glaucoma at the time of the primary screening seven (10 eyes) were followed up. Additional progression was recorded in half of these eyes despite treatment and a pressure level of 20-24 mm Hg while in the other half the conditions had remained unchanged. In two of the latter eyes the pressure level was above 25 mm Hg. All in all these findings stress the bad prognosis for eyes presenting a rather extensive glaucomatous field loss.

Glaucoma according to the chosen criteria was unilaterally present in ten of the patients followed up. Six of these had both eyes treated. Only a single patient had developed visual field defects of the non glaucomatous eye.

Borderline cases The age and sex distribution of 48 patients is seen in table 1.

43 patients remained untreated during the observation period and visual field measurement and ophthalmoscopy revealed no glaucomatous changes in these cases. An altered characterisation in keeping with the stated criteria must therefore be based solely on the pressure values during the observation period.

It is shown in table 5 that during the observation period pressure levels below 20 mm Hg were recorded in 17 eyes without treatment but only in four patients in both eyes. In conformity with the criteria employed these latter borderline cases should be characterized as normal after the follow up.

Table 5 also shows that during the observation period pressure levels of 25 mm Hg or higher were recorded for four eyes (three patients). These eyes all

Table 5
Pressure level during the observation period in 48 patients (96 eyes) characterized as borderline cases

pressure level	without treatment	with treatment	Total
< 20 mm Hg	17	1	18
20-21 mm Hg	38	4	42
22-24 mm Hg	27	5	32
≥ 25 mm Hg	4	-	4
Total	86	10	96

clinic, *Centralsygehuset Nykøbing Falster* including both the 169 patients whose screening tension had been measured at 20 mm Hg or higher and the ten other patients suspected of glaucoma after the screening

A five year assessment of the course for the 1703 patients characterized as normal after routine tonometry was based solely on data from the case records of the only ophthalmologist of the island

1 Follow Up ■ the Patients who at Routine Tonometry had a Screening Tension of 20 mm Hg or higher

Of the 169 patients 46 had died within the observation period while in the cases of 13 patients a five year follow up examination could not be carried through for different reasons

The number of patients subjected to a five year follow up examination was thus reduced to 110 of whom 42 were under treatment while 68 were untreated

A. Patients Subjected to a Five-Year Follow Up

This group comprised as stated 110 patients practically all examined in the Department of Ophthalmology *Centralsygehuset Nykøbing Falster* 104 by the author in person These patients represented 63 per cent of the original 169 found to have an intra ocular pressure of 20 mm Hg or higher

The follow up examination included determination of the central visual acuity ophthalmoscopy campimetry (preferably object sizes 2/2000 and 6/2000) and applanation tonometry The examinations were performed at different times of the day according to the desires of the individual patients

Where possible the examination was supplemented by data from the ophthalmic consultations within the observation period The number of control examinations by the ophthalmologist varied considerably While thus 33 patients (32 per cent) failed to attend for control among whom however only three with a diagnosis of glaucoma 43 patients had attended from 10 to 26 times

Though we must reckon with failing attendance for control by some of the patients – in the present series one third – the survey of the number of control consultations within the observation period illustrates the great work with which the ophthalmologist going in for routine tonometry is nevertheless burdened

The age and sex distribution of the 110 patients followed up is shown in table 1 96 were males and 84 females The youngest patient was 41 years old and the oldest 86 (average age 66)

Table 1 also illustrates the distribution according to diagnosis It is seen that 50 cases were diagnosed as glaucoma while 48 were characterized as borderline cases and finally 12 as normal

gression One patient with previously normal conditions who failed to appear for control developed visual field defects

C Patients Dead Within the Observation Period

46 patients died within the observation period. These constituted 27 per cent of the 169 subjected to further examination. The mortality was 60 per cent for patients aged over 75. Half of the 46 patients had died before the elapse of three years. The relatively few data available must be considered in assessing the course in this group. Half of the patients had, it is true, consulted an ophthalmologist less than six months before death, but 13 had not been seen for control.

Four patients under treatment who had glaucoma at an advanced stage presented with a single exception further development of their visual field defects and one patient had become blind of both eyes. To judge from the data available none of the other patients had shown any glaucoma provoked changes of the state.

D Further Course in Patients Aged Over 75

As stated above a considerable number of the patients aged over 75 had died within the observation period. A separate assessment was therefore desirable of the conditions in the 42 patients aged over 75 at the time of the screening. It appeared that 25 patients had died. Five could not be followed up while 12 were subjected to follow up examination.

Of the 42 patients 14 had been under treatment but only in two cases with a resulting regulation of the tension to below 20 mm Hg. Five patients under treatment and with glaucomatous field loss presented further progression of the disease. In one case glaucomatous field loss was seen in a patient with originally normal conditions (case 2).

E Development of Blindness Within the Observation Period

Of the 110 patients followed up two - males aged 50 and 74 respectively - had become blind within the five year observation period according to the definition of blindness indicated by the Danish Society for Blind Welfare (a visual acuity not exceeding 4/60 or a visual field below 20° and combinations of these defects). These patients both had central vein thrombosis in addition to glaucoma.

Among the 46 patients dead within the observation period further information on development of blindness was available in three cases. In only one of these - a woman aged 87 - was the blindness due to glaucoma. One of the other

Table 1
Age and sex distribution and characterisation of 110 patients followed up

age	glaucoma diagnosed		borderline cases		normals		Total	
	males	females	males	females	males	females	males	females
35-44	—	—	1	3	—	1	1	4
45-54	2	2	4	5	—	2	6	9
55-64	6	6	—	11	—	2	6	19
65-74	5	13	3	11	1	4	9	28
75-84	1	11	1	7	—	2	2	20
≥ 85	1	3	1	1	—	—	2	4
Total	15	35	10	38	1	11	26	84

Results

In assessing the results there is reason to concentrate in the first place on the question of the chances the individual methods of examination have of prognosticating the further course

Anamnestic data On the primary tracing we tried to single out a group among the patients subjected to further examination on the basis of our knowledge concerning a relationship between glaucoma and central vein thrombosis glaucoma and diabetes glaucoma and high myopia glaucoma and thyroid dysfunction and glaucoma and pseudoexfoliation (Becker & Shaffer 1965) Of the 25 patients constituting this group only 12 had follow up examination carried through 12 had died within the observation period among whom nine out of 12 with diabetes mellitus This is a factor to be considered together with the patient's age when deciding on the extent of the further examinations and possible institution of treatment of diabetics

Of the 12 patients followed up nine had glaucoma for which they had been treated during the observation period Progressive glaucoma occurred in two out of four patients with combined central vein thrombosis and glaucoma The others showed no change

Seven out of eight patients who gave information on a familial predisposition were subjected to follow up examination Five patients under treatment had glaucoma of whom four with greater or smaller visual field defects Progression of the glaucoma during the observation period was noticed in one case only

To judge from the present investigation information on a familial predispo

period and only one had an alteration recorded of the pressure level to 25 mm Hg or higher. One patient who presumably would have been caught by presence of glaucoma suspicious optic discs showed unaltered beginning visual field defects.

By raising the screening level to 22 mm Hg 60 patients would not have been suspected of glaucoma on routine tonometry. Ten patients were treated during the observation period but only half obtained regulation of the tension to be low 20 mm Hg. Four of the treated patients presented visual field defects. Two of these had developed a more advanced glaucoma. In four untreated patients a rise of the pressure level to 25 mm Hg or higher was recorded. In 52 cases the state had remained unchanged.

By raising the screening level to 25 mm Hg 81 of the 110 patients followed up would not have been suspected of glaucoma. 17 of these were treated during the observation period with a resulting fall of the pressure level to below 20 mm Hg in five. Visual field defects were seen in six of the treated patients of whom four presented glaucoma at an advanced stage. Seven untreated patients had rises of the pressure level to 25 mm Hg or higher recorded. 68 of the 81 patients displayed no glaucoma provoked changes of the state.

By raising the screening level to 22 mm Hg for patients ranging in age from 35 to 64 a total of 41 patients would not have been suspected of glaucoma on routine tonometry. Eight patients were subjected to treatment of whom two had the tension regulated to below 20 mm Hg. None of the 41 patients had developed visual field defects within the observation period. One of those not treated had a rise of the pressure level to 25 mm Hg or higher recorded. One patient who presumably would have been caught by presence of glaucoma suspicious optic discs displayed unaltered beginning visual field defects.

If the screening level had been raised to 25 mm Hg for patients over 65 years of age 27 of the patients followed up would not have been suspected of glaucoma on routine tonometry. Five of these patients had been treated with the result that two had obtained a regulation of the tension to below 20 mm Hg. Among the treated patients four displayed visual field defects of whom two had glaucoma at a fairly advanced stage. In two patients subjected to no treatment the pressure level recorded had risen to 25 mm Hg or higher. In the remaining 21 of these 27 patients no change of the state due to glaucoma was noticed.

B Patients Not Subjected to a Five Year Follow Up

In the cases of 13 patients follow up examination could not be carried through from different causes. In general only few data were available for this group. Two patients had therapy instituted with a resulting regulation of the tension to below 20 mm Hg but in only one of these was it possible to prevent pro

sition and occurrence of central vein thrombosis are the factor of the greatest value in tracing glaucoma

Pressure level Table 2 shows a recording of the pressure levels during the observation period for all the 110 patients (220 eyes) based on measurements at the follow up supplemented by measurements carried out by the ophthalmologist within the observation period. Of the 110 patients 68 were untreated while two had only one eye treated.

Among the 68 patients a pressure level of 22 mm Hg or higher was recorded for 46 eyes or 33.3 per cent.

Among 42 patients who had treatment instituted a pressure level below 20 mm Hg was obtained for no more than 13 eyes (18.3 per cent) while in half of the cases (52.4 per cent) levels of 22 mm Hg or higher were recorded.

In table 3 the pressure levels recorded on the further examination in the ophthalmic unit following the original examination is compared with the levels found at the follow up for 68 patients (136 eyes) given no treatment. It is seen that in 61 eyes (49.3 per cent) the pressure level was unaltered. A lower level was recorded for 15 eyes (11.0 per cent). However only two obtained a fall from 25 mm Hg or higher to within the range of 20-24 mm Hg and only one a fall from 25 mm Hg or higher to below 20 mm Hg.

A higher pressure level at the follow up was recorded for 54 eyes (39.7 per cent) but only nine showed a rise from the 20-24 mm Hg range to 25 mm Hg or higher and in only a single case was a rise noticed from below 20 mm Hg to 25 mm Hg or higher.

The pressure values compared originating from single measurements which need not have been carried out at the same time of the day, the conclusions we may be justified in drawing are limited. Evidently however no definite change towards a higher pressure level occurred during the observation period. Similar shifts towards both higher and lower pressure values as in the present series have been recorded by Linner & Stromberg (1964), Leydhecker (1966) and the

Table 4
Pressure level during observation period in 220 eyes (110 patients)

	< 20 mm Hg	20-24 mm Hg	25-29 mm Hg	≥ 30 mm Hg	Total
without treatment	41	51	31	15	138
with treatment	15	24	34	9	82
Total	56	75	65	24	220

Table 6
Age and sex distribution of 333 previously normal patients who had their intra ocular pressure measured on consulting the ophthalmologist with in the observation period

age	males	females	Total	pressure level					
				20-21 mm Hg		22-24 mm Hg		≥ 25 mm Hg	
				males	females	males	females	males	females
35-44	9	82	41	1	-	-	-	-	-
45-54	23	68	91	1	6	-	-	-	-
55-64	9	44	53	-	5	9	4	-	2
65-74	6	26	32	4	5	-	2	-	1
75-84	3	2	5	-	2	-	-	-	1
Total	50	172	222	6	19	2	6	-	4

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(Head Prof Tibor Nony)*

CANALICULOPLASTY

BY

IMRE KORCHMÁROS

This is a brief report on some of our procedures for lacerated or obstructed lacrimal canaliculus

The procedures were mostly performed in block anaesthesia

In cases of lacerated canaliculi if the torn end of the nasal stump is invisible a few drops of fluid (e.g. adrenaline chloramphenicol eye drops) are dropped into the wound and the patient is asked to blow out air through the nose while his nostrils are compressed. As it is well known to everybody sometimes air bubbles appear in the fluid (1, 2) indicating the torn end of the nasal stump. If they do not air is injected from a syringe through the intact canaliculus. Obviously the lower part of the lacrimal sac must be blockaded by a suitable blunt tool pressed onto the skin (Fig. 1) as it is made at retrograde irrigation for canaliculitis (3).

The so called retrograde procedure can also be performed by using the retrograd cannula (4). This spiral formed canule (Fig. 2) is introduced from the intact canaliculus into the lacerated one. Thus air or fluid can be injected directly into the lacerated canaliculus in order to find the torn end (Fig. 3). The syringing itself makes it easier to drive the retrograd cannula.

The retrograd cannula may be used simultaneously for the reconstruction too. After a few rotations the tip of the canule appears in the torn end of the lacerated canaliculus. Then a plastic thread is inserted into the canule (Fig. 4) the instrument is withdrawn the thread is inserted into the temporal

- Midtvedt T* Acta Paed scand 54 81 85 1965
- Perkins E S* Uveitis and toxoplasmosis J & A Churchill Ltd London 1961
- Ramsell T G & Gamero B A* Brit J Ophthal 51 282 283 1967
- Rieger H* Die Augenveränderungen bei der Toxoplasmosis acquisita in Toxoplasmosis Georg Thieme Verlag Stuttgart 1962

two patients had become blind owing to senile macular degeneration and the other to proliferative diabetic retinopathy

Blindness was thus recorded for five patients but in one case only was glaucoma the sole cause of this

II Follow Up of Patients Suspected of Glaucoma Despite a Screening Tension Below 20 mm Hg

This group comprised ten patients, of whom seven were followed up. In agreement with the results of the original further examinations no signs of glaucoma were seen in this group consisting mainly of patients who on routine tonometry had shown a difference exceeding 4 mm Hg between the right and the left eye

III Course in the Patients Characterized as Normal on Routine Tonometry

1703 patients were characterized as normal on the basis of routine tonometry. For this group a five year follow up was impossible to carry through. An attempt was made instead to judge of the further fates of these patients by utilizing the data procurable from the case records of the only ophthalmologist of Falster

These showed that 538 of the 1703 patients (32 per cent) had consulted the ophthalmologist within the observation period. Similarly as noted for the routine tonometry the number of females attending for renewed examination exceeded that of males being 36 per cent (389 females) and 24 per cent (149 males) respectively. The age distribution was fairly uniform though with the lowest representation of the age groups of 35-44 and 75-84

The patients were examined in accordance with the causes of their consulting the ophthalmologist. Ophthalmoscopy showed normal optic discs in all cases. On the examination no special point was made of having the intra ocular pressure recorded again. Therefore (table 6) only 222 patients (50 males and 172 females) corresponding to 41 per cent of those attending or 13 per cent of the original 1703 patients were subjected to renewed applanation tonometry

Table 6 shows the age and sex distribution of 36 patients who had an intra ocular pressure of 20 mm Hg or higher recorded within the observation period. The mean age at the time of control pressure measurement was 61 the youngest patient being 44

The incidences of pressure values ≥ 20 mm Hg ≥ 22 mm Hg and ≥ 25 mm Hg were 16.2 per cent (36 patients), 5.4 per cent (12 patients) and 1.8 per cent (4 patients) respectively. The highest intra ocular pressure recorded was 27 mm Hg. No patient aged under 55 had an applanation value of 22 mm Hg or higher measured

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THE EFFECT OF TRACHOMA ON INTRAOCULAR TENSION

BY

P AWASTHI and H P S BHATIA

Trachoma as a source of human suffering a cause of blindness and as such causing economic loss over large tracts of the World is second to none amongst the diseases of the eye or indeed diseases of all kinds

It is a specific contagious disease of chronic nature the course of which is prolonged and the tendency towards gradual healing by fibrosis is almost a uniform feature Taking this fibrosis into view some workers have reported in favour of a relationship between trachoma and ocular hypertension Investigators like *Wecker* (1900) *Mc Callen* (1936) *Sedan* (1939) and *Boles Carenini & Combiaggi* (1957) have shown that the frequency of glaucoma is definitely higher in trachomatous subjects than among non trachomatous On the other hand *Guarino* (1914) *Lagrange* (1922) *Terson* (1928) *Trantas* (1937) and *Pasion* (1957) advocate that the two conditions are independent However the factor of scleral rigidity has not been taken into account by these workers and higher rigidity might have given rise to erroneous diagnosis of glaucoma Hence 141 cases of trachoma were subjected to tonometry Moreover scleral rigidity was also derived firstly to assess the effect of trachoma on ocular rigidity and secondly to avoid false tonometric conclusions

Material and Methods

The patients for the present study were those attending the department of Ophthalmology S N Medical College Agra These cases were either suffering from trachoma or had suffered from trachoma

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bers of the donor corps of Falster traced by applanation tonometry (Norskov 1970a) Further they are supported by more summary statements based on follow up examinations by Bertelsen (1965) Norskov (1967) Fruhauf *et al* (1968) and Graham (1968)

The assessment is more difficult where the treated patients are concerned Of the 42 treated patients showing normal conditions at the primary screening only three developed glaucomatous field loss (cases 1-3 pp 879-880) These ranged in age from 68 to 76 at the time of the primary screening In one of these patients the screening tension of the eye concerned was 19 mm Hg being thus below the screening level This patient had been caught by a screening tension of 21 mm Hg of the opposite eye

A similar problem regarding treated and untreated patients subjected to follow up examination presented itself in the follow ups carried out by Leydhecker (1960b 1966) after three and seven years respectively A comparison of the results achieved may be of interest though the patients were selected constituting groups from ophthalmic practice and employees of a business respectively

It is remarkable that Leydhecker (1960b) on a follow up examination of glaucoma patients after three years of observation recorded glaucomatous field loss in 32.5 per cent of those with previously normal visual fields The present investigation showed such a development in no more than 7 per cent of the treated patients and in none of the untreated

In assessing the course in the treated patients we must bear in mind that of course the treatment can only be expected to have effect if it really does bring about a fall of the pressure A regulation to below 20 mm Hg is supposed to be required (Weekers *et al* 1959 Goldmann 1960 Lawwitz 1960 Touvinen 1961 Leydhecker 1963 Shaffer 1967 Sugar 1969)

It has however been noticed often to be difficult to obtain a fall in eyes with a pressure level about 25 mm Hg which in fact will predominate among patients traced on examinations for revealing glaucoma (Goldmann 1960 Walker 1966 Leopold 1967)

In agreement with this the present investigation showed that an ideal normalisation to below 20 mm Hg was obtained in no more than 18 per cent of the treated eyes while a pressure level of 22 mm Hg or higher was present in 52 per cent Progression of the visual field defects was seen in 17 per cent (14 eyes) of the total number treated

Leydhecker (1966) at the follow up after seven years likewise recorded pressure levels of 22 mm Hg or higher in two thirds of treated or untreated glaucoma cases whereas progression of visual field defects was noticed in 40 per cent of the total number of glaucoma cases

A comparison of the two materials is actually unrealistic If nevertheless one will attempt to give a possible explanation of the considerable difference between the assessments of the further course for patients traced by routine

The clinical examination of both the eyes was done firstly by oblique illumination and then by the slit lamp. The main aim was to examine the lids for any sequela of trachoma conjunctiva for follicles and scarring and lastly cornea for pannus scarring and opacities etc.

On the basis of above examination the patients were categorised according to the WHO classification of trachoma.

As a control case 51 medical students of both the sexes were examined who were free from trachomatous infection clinically.

The intraocular pressure of these patients was recorded by paired tonometry to establish the scleral rigidity in addition to the ocular tension.

Observations

A total of 141 cases belonging to various stages of trachoma were examined. The age of these patients were between 10 to 40 years which is presumably the preglaucoma age.

Fig 1 shows the stages of trachoma and the age group of the 141 patients of the present study.

The intraocular tension above 22 mm Hg in eight patients (5.67%) mostly belonging to IV stage definitely categorises these patients into suspicious group of glaucoma cases which alarms for a thorough checking and constant supervision time to time.

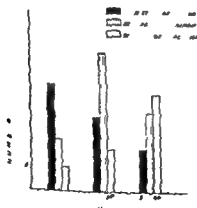


Fig 1

Showing cases of various age groups in different stages of trachoma

On the basis of the data available and referring to the criteria chosen a diagnosis of glaucoma but without field loss was established in two women aged 62 and 64 respectively. In the other two cases in which a pressure value of 25 mm Hg or higher had been measured within the observation period control measurements gave a pressure level below 25 mm Hg.

Discussion and Conclusion

Through the present investigation it has been aimed at giving the best possible illustration of the further course during a five year observation period within a group of patients aged over 35 who had consulted an ophthalmic medical practitioner. This group comprised 169 patients with an intra ocular pressure of 20 mm Hg or higher, 10 patients whose condition also raised suspicion of glaucoma and finally 538 patients characterized as normal who re consulted the ophthalmologist within the observation period.

Of the 169 patients 110 or 65 per cent were followed up while 46 had died within the observation period and 13 could not be followed up for different reasons.

A very important question in a follow up of this kind is that of the course without treatment in a group of patients suspected of glaucoma after routine tonometry.

No direct answer can be given to this question on the basis of the present investigation. For ethical reasons the ophthalmologist had to offer treatment when the glaucoma diagnosis had been established according to the chosen criteria. In addition at the time of the primary screening treatment of patients without glaucomatous field loss was insisted on (Schmidt 1960, Leydhecker 1960b, 1963).

Of the 110 patients followed up 42 were consequently under treatment and 68 untreated.

Among the 68 untreated patients none had developed glaucomatous field loss during the observation period. The extent of the visual field defects had remained unchanged in one patient.

To judge from the course in the 68 untreated patients the chance that patients with a mild ocular hypertension will develop glaucomatous field loss within a five year period seems to be small. This is in agreement with the views previously advanced by Linnér & Strömberg (1964, 1967) based on follow up examinations after two and five years of untreated persons with ocular hypertension. These results are borne out by those of follow up examinations carried through by Haas (1967) and Armaly (1969) and those of a five year follow up performed by the author on the same lines as the present among mem-

The values of corrected tension and the coefficient of scleral rigidity were expressed according to the table of Becker & Shaffer

These patients were put into the following groups on the basis of corrected tension

- 1 Group A – Patients with the tension above 22 mm Hg
- 2 Group B – Patients between the tension 19-21 mm Hg
- 3 Group C – Patients with a tension below 19 mm Hg

Fig 2 shows the distribution of the cases into these various groups –

Discussion

In severe cases of trachoma and especially in repeated reinfection the whole circumference of the cornea becomes vacularised infiltrated and finally scarred. Implication of the aqueous veins in the trachomatous infiltrative process or worse still in the trachomatous scarring of the limbic and paralimbic regions might lead to an impediment to the outflow of aqueous humour and a consequent rise of the intraocular pressure.

As described 141 cases of trachoma were subjected to paired tonometry. The coefficient of scleral rigidity and the intraocular tension were expressed according to the table of Becker & Shaffer.

It was observed that out of 141 cases 8 patients (5.67%) showed a definite rise of tension above 22 mm Hg. The mean value of tension was 24.25 with

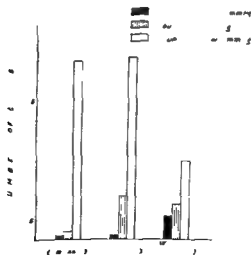


Fig 2

Showing intraocular tension in various stages of trachoma

development of visual field defects were noticed in ten patients (14 eyes). Seven of these would however probably have been caught by ophthalmoscopy presence of central vein thrombosis or elucidation of a familial predisposition a circumstance which stresses the importance of these factors in glaucoma tracing. On the other hand to judge from the results of the present investigation the water provocative test yielded no prognostic suggestions neither for patients displaying additional glaucomatous field loss during the observation period nor for patients with a rising pressure level to an arbitrarily chosen pathological value of 25 mm Hg or higher in the course of the observation period. The same impression that the water provocative test has a very limited possibility of prognosticating the further course has been stated by Armaly (1969) and by the author on the basis of a previous follow up study (Norskov 1970a).

It would be well if the results of the present investigation might serve to suggest a modification of the screening procedure so as to reduce the number of patients suspected of glaucoma and at the same time facilitate encircling of patients being particularly liable to develop visual field defects. In the present investigation similarly as at the primary screening it was chosen to study the consequences of altering the screening level to ≥ 21 mm Hg ≥ 22 mm Hg and ≥ 25 mm Hg respectively and to undertake a graduation according to age using a screening value of 22 mm Hg or higher for the age group of 35-64 and 25 mm Hg or higher for that over 65.

Reservation must in any case be made with regard to reflections of this kind with a view to suggestions for altering the glaucoma screening procedure on the basis of a limited series of patients. The problem to be considered is in fact that of the margin of security with which one desires to work within the field of glaucoma screening provided one attributes a central position to routine tonometry. If we may be justified in drawing certain conclusions on this basis it seems that choice of 21 mm Hg as the screening level may be permissible. This has in fact often been indicated as an appropriate screening level when applanation tonometry is employed (Goldmann 1960 Schmidt 1960 Becker & Shaffer 1965 Chandler 1965 Leopold 1967 Pollack 1964).

The results of the present investigation also suggest that a screening level of 23 mm Hg might be considered for patients ranging in age from 35 to 64. On the other hand the remaining suggestions for altering the screening level probably cannot be insisted on without definitely departing from the fundamental principles of routine tonometry.

Another possibility of improving the screening procedure might be based on the fact that 60 per cent of the patients aged over 75 had died within a five year period. A review of this group disclosed that all the patients presenting further development of glaucoma during the observation period also had had glaucomatous or glaucoma suspicious optic discs recorded on the primary screening. However at the same time it was noticed that one of the three patients who

standard deviation of 0.75. This rise in ocular pressure was statistically significant ($0.001 < 0.005$). The maximum number (6) of these patients belonged to IV stage of trachoma and only one case of II stage and one case of III stage (Fig. 2). The maximum rise of tension in as many as six cases in IV stage suggests that fibrous and scarring in this stage plays a vital role to make the eye prone to be hypertensive. It has been suggested that trachomatous scarring hinders in the outflow of aqueous presumably affecting the aqueous veins.

In cases of IV stage of trachoma there was an apparent rise in coefficient of rigidity with an average of 0.0234 and a standard deviation of 0.0072. But statistically this change was insignificant ($0.001 < 0.005$) (Fig. 3).

77 cases (15.60%) out of 141 patients presented with a tension between 19 to 21 mm Hg (Average 19.77 and standard deviation 1.04). In these cases the ratio was higher in IV stage of trachoma. The coefficient of scleral rigidity in these cases was within normal limits statistically (average 0.0232 standard deviation 0.0071).

Rest 111 cases present with an ocular tension below 19 mm Hg (average 14.97 and standard deviation 2.91). Their mean ocular rigidity was 0.0225 (standard deviation 0.0069) which was normal statistically.

In control group the mean intraocular tension was 14.41 mm Hg (Standard deviation 4.6) and the mean value of ocular rigidity was 0.0227 (standard deviation 0.0068).

It is suggested therefore that the tension must be recorded in all the cases with trachoma especially in late stages to discover unsuspected cases of glaucoma.

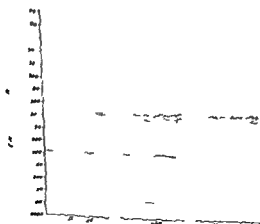


Fig. 3

atterogram showing distribution of scleral rigidity in various stages of trachoma.

tonometry based on the two investigations attention may be called to the fact that Leydhecker's series included a greater number of glaucoma patients with field loss at the primary screening. In this connection it may be mentioned that among seven followed up patients of the present series who displayed a fairly extensive field loss at the primary screening further progression had developed in half of the eyes.

Another question suggesting itself is whether it may be possible to clarify on the basis of the present investigation whether patients traced by routine tonometry but without glaucomatous field loss are particularly liable to develop field loss within a five year observation period compared with patients characterized as normal on routine tonometry.

Various factors render a direct comparison difficult. First only 32 per cent of the 1703 normals were subsequently examined by an ophthalmologist and no more than a scant half of these were subjected to tonometry. Secondly as stated above only 68 of the 110 patients followed up had remained untreated while in the remaining 42 patients the course was influenced by the instituted therapy.

A follow up examination of normals disclosed no cases of glaucoma with field loss while both pressure values above the chosen screening level (20 mm Hg) and rises to 25 mm Hg or higher (an arbitrarily chosen pathological level) were recorded. Similar results were achieved by the author on previous follow up examinations of patients characterized as normal after tonometry among patients admitted to a medical unit (Nørskov 1967) and among members of the blood donor corps of Falster (Nørskov 1970a). This is also in agreement with Linner & Strömberg's experience based on a five year follow up of 659 persons born between 1896 and 1905 who originally had a tension value of 4 0/5 5 or higher. Further Armaly (1969) who closely followed for up to ten years a defined normal group comprising 3936 persons could only in four cases disclose visual field defects to be characterized as glaucomatous on the basis of the chosen criteria.

Compared with this none of the 68 untreated patients included in the present study presented glaucoma with field loss while as in the normal group rises to pressure levels of 25 mm Hg or higher were recorded.

If one chooses instead to base the comparison on the borderline cases - five treated and 43 untreated patients - singled out on the primary screening as a special risk group two patients were in fact found to have developed glaucoma with field loss. Note however that in one of these two cases the discs had originally been characterized as glaucoma suspicious. The case was however according to the chosen criteria referred to the group of borderline cases.

That a group which is liable to develop visual field defects must be included among the patients singled out by routine tonometry in ophthalmic practice is evident from the fact that despite treatment presence of or further de-

Summary

141 cases of trachoma were studied with a view to find out if trachoma could give rise to increased ocular tension. Scleral rigidity was also derived in these patients lest there might be a wrong tonometric conclusion. 5.67% of the eyes recorded a tension above 22 mm Hg while their scleral rigidity was normal statistically. Hence the importance of thorough investigation of trachomatous cases especially late stages to exclude glaucoma has been stressed.

References

- 1 Boles Carenini B & Cambiaggi A (1957) *Rev Int Trach* 1 61
- 2 Guarino (1914) Cited by (1)
- 3 Wecker A de (1900) *Ann Oculist (Paris)* 124 45
- 4 MacCallan A F (1936) *Trachoma* p 53 Butterworth London
- 5 Sedan J (1939) Cited by Larmande & Lengo (1960) *Ibid* 37 p 265
- 6 Terson A (1928) *Bull Soc France Ophth* 41 329
- 7 Trantas A (1937) *Rev Int Trach* 13 131
- 8 Lagrange F (1922) Cited by Larmande & Lengo (1960) *Ibid* 37 p 265

velopment of visual field defects were noticed in ten patients (14 eyes). Seven of these would however probably have been caught by ophthalmoscopy, presence of central vein thrombosis or elucidation of a familial predisposition a circumstance which stresses the importance of these factors in glaucoma tracing. On the other hand to judge from the results of the present investigation the water provocative test yielded no prognostic suggestions neither for patients displaying additional glaucomatous field loss during the observation period nor for patients with a rising pressure level to an arbitrarily chosen pathological value of 25 mm Hg or higher in the course of the observation period. The same impression that the water provocative test has a very limited possibility of prognosticating the further course has been stated by Armaly (1969) and by the author on the basis of a previous follow up study (Norskov 1970a).

It would be well if the results of the present investigation might serve to suggest a modification of the screening procedure so as to reduce the number of patients suspected of glaucoma and at the same time facilitate encircling of patients being particularly liable to develop visual field defects. In the present investigation similarly as at the primary screening it was chosen to study the consequences of altering the screening level to ≥ 21 mm Hg, ≥ 22 mm Hg and ≥ 25 mm Hg respectively and to undertake a graduation according to age using a screening value of 22 mm Hg or higher for the age group of 35-64 and 25 mm Hg or higher for that over 65.

Reservation must in any case be made with regard to reflections of this kind with a view to suggestions for altering the glaucoma screening procedure on the basis of a limited series of patients. The problem to be considered is in fact that of the margin of security with which one desires to work within the field of glaucoma screening provided one attributes a central position to routine tonometry. If we may be justified in drawing certain conclusions on this basis it seems that choice of 21 mm Hg as the screening level may be permissible. This has in fact often been indicated as an appropriate screening level when applanation tonometry is employed (Coldmann 1960, Schmidt 1960, Becker & Shaffer 1965, Chandler 1965, Leopold 1967, Pollack 1967).

The results of the present investigation also suggest that a screening level of 22 mm Hg might be considered for patients ranging in age from 35 to 64. On the other hand the remaining suggestions for altering the screening level probably cannot be insisted on without definitely departing from the fundamental principles of routine tonometry.

Another possibility of improving the screening procedure might be based on the fact that 10 per cent of the patients aged over 75 had died within a five year period. A review of this group disclosed that all the patients presenting further development of glaucoma during the observation period also had had glaucomatous or glaucoma suspicious optic discs recorded on the primary screening. However at the same time it was noticed that one of the three patients who

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AQUEOUS LEAKAGE THROUGH THE UVEAL VESSELS - A FACTOR IN CHOROIDAL DETACHMENT?

BY

BENGT ROSENGREN

The kind of choroidal detachment seen after operations for glaucoma and cataract was first studied systematically by *Fuchs* in 1900 and 1902. Its incidence after cataract operations was stated to be 4.7 per cent and that after iridectomy 10 per cent. This condition - including ocular hypotension, abolished anterior chamber and choroidal detachment - was attributed to postoperative lesions by *Fuchs*. In some eyes examined histologically after cataract operations *Fuchs* observed rupture of the iris root at the point of attachment of the ciliary body to the sclera, and he concluded that this enabled aqueous humor to be transported to the suprachoroidal region.

In 1917 *Meller* advanced a theory with other aspects. In his opinion a post-operatively persistent fistula to the exterior was a significant factor. This would lead to leakage of aqueous humor and/or fluid from the vitreous and subsequent vitreous shrinkage. *Meller* took into account the fact that choroidal detachment predominantly occurs at high age levels, something he attributed to the greater scleral rigidity exhibited in these age groups. Together with this higher rigidity shrinkage of the vitreous would be responsible for the choroidal detachment.

Hagen (1970) subscribed to the view of an external fistula as a significant factor. This explanation was sufficient in those cases in which an external fistula was present which, among other things, appeared from the rapid disappearance of the symptoms - hypotension, abolished anterior chamber and choroidal detachment - as soon as the fistula could be closed. *Hagen* postulated that in those cases where no direct external fistula could be demonstrated an

developed glaucomatous field loss despite normal conditions at the primary screening actually belonged to this age group

Nevertheless it is tempting to aim at modifying the glaucoma screening procedure by forbearing routine tonometry in the cases of patients aged over 75 because one should in any case be reserved with regard to administering miotics to patients of this age class unless glaucomatous field loss is present

If finally we consider the age at the time of routine tonometry of the patients with visual field defects at the follow up we see that nine out of 12 patients with simple glaucoma and field loss ranged in age between 59 and 71. This is the age group which Strömberg (1962) among others pointed out as the group most liable to development of an intra ocular pressure above 25 mm Hg. This means that no matter which glaucoma prophylactic measures one prefers to go in for special attention should in addition be concentrated on the stated age group.

Employment of routine tonometry will further as in the present study involve that a considerable number of patients from the group with ocular hypertension are singled out as glaucoma cases according to the current criteria and consequently treated. In the present study it could not fail to impress one that several of the treated patients without glaucomatous field loss expressed complaints of a rather massive visual impairment. A very thought provoking description of these therapeutic troubles has been given by a colleague under the name of "the miotic life" (1964). A concurrent cause of these therapeutic complaints was doubtless the fact that in the endeavours to obtain an ideal normalisation below 20 mm Hg the group of patients concerned was an intensely treated one but that as stated normalisation was nevertheless obtained in a small number of cases only.

Within recent years however the attitude held towards treatment of glaucoma without field loss seems to have altered. While previously as expressed by Schmidt (1960) and others the view was adhered to that treatment ought to be instituted when the intra ocular pressure exceeded 22 mm Hg the pressure range of 25–30 mm Hg now seems to be preferred unless glaucomatous field loss is present (Chandler 1965, Shaffer 1967, Leopold 1967, 1969, Snyderker 1969). Such an altered attitude must necessarily influence the placing of routine tonometry within the glaucoma prophylactic work.

Conclusive remarks In evaluating the results achieved we must bear in mind that the observation period was five years only and that therapy had been instituted in some cases while on the other hand one fourth of the glaucoma suspects were recorded to have died within the observation period and an ideal normalisation to below 20 mm Hg had been obtained for a small proportion only of the treated patients despite intensive therapy.

Our main impression of the investigation reported above must be that the very considerable number of patients with ocular hypertension who on routine

occult external microfistulation served as a similar causative factor *Hagen* stated that the incidence was 22 per cent after cataract operations and 76 per cent after Elliot trepanation

Hagen was able to demonstrate that the suprachoroidal fluid was neither aqueous humor nor vitreous humor but a fraction much richer in proteins probably a transudate from the choroidal induced by the low pressure This statement has later been confirmed by *O'Brien* and by *Dobree* who using more modern techniques found an albumin value of 0.3 per cent

In a paper published 1961 *Chandler & Maumenee* drew attention to the fact that choroidal detachment frequently occurs under conditions incompatible with the presence of an external fistula for example cases in which the condition becomes manifest a long time after the operative intervention They discussed, from this point of view whether a function of the ciliary body's secretory activity might not result from primary low detachment of the ciliary body

Nevertheless the generally accepted view whenever no external fistulation can be demonstrated seems to be that some form of occult external microfistulation is present However the following case which recently came my way seems to suggest another possible explanation

A female patient aged 73 with an advanced glaucoma in both eyes

V r 5/7 (+0.50) T appl r 38 1 45
l 5/10 (\pm 0)

Visual fields r central rest 10° (Bjerrum 4/1000) l central rest 5° (Bjerrum 4/1000)

Despite maximal drug therapy for glaucoma the tension could not be normalized

Right eye

29/1 iridencleisis according to Stallard

12/2 normal healing conjunctival sutures removed

14/2 bleb at 12 o'clock T = 10/5.5

18/2 low bleb at 12 o'clock T = 10/5.5

3/3 V = 5/10 (+1.0) Barely manifest bleb T = 15/5.5

Choroidal detachment nasally at the margin

17/3 V 5/10 (+1.0) Shallow anterior chamber T = 13/5.5 High choroidal detachment

Attempts were ineffectively made with Pilocarpine \times 3 and later Corotone \times 3
25/5 It was noted in the records that the patient's vision 3 days previously was so reduced that she could not discern the windows Now the tension previously barely measurable had risen to appl 32 and V = 5/10 Given Diamox After some days T dropped to 0 and the choroidal detachment returned and became total

8/4 V = 0 T = 17/5.5 The choroidal detachment was total so it was decided to carry out

8/4 *Pyrodiathermy** over the iridencleisis region

9/4 No definite improvement Chamber remained extremely shallow and T = 10/5.5

Tension measurements on subsequent days repeatedly showed that in about 5 seconds T dropped from 12/5.5 to 15/5.5 The conjunctiva had healed and the bandages after

* Diathermy combined with cooling of the surface by means of ice cold distilled water dropped around the ball electrode

tonometry became suspected of glaucoma but otherwise presented normal conditions would have no great chance of developing glaucomatous field loss within a five year observation period. Glaucomatous field loss was mainly found among the patients showing this defect at the primary screening among patients with central vein thrombosis and among patients with a familial predisposition. Finally the present investigation also showed that patients with ocular hypertension at the follow up were recruited even from the group acquitted of glaucoma suspicion on routine tonometry.

The suggestions advanced on the basis of this study with a view to modifying the screening procedure though with consistent employment of routine tonometry and at the same time obtaining a more effective encircling of the patients liable to develop glaucomatous field loss showed that any alteration whether great or small would add to the risk of missed glaucoma cases and consequently to a limitation of the glaucoma prophylactic value of routine tonometry.

Finally to judge from the results of the present investigation it seems as if the most effective efforts against development of damages due to glaucoma must still consist in transferring as much as possible of the work required to carry through routine tonometry on an intensification of control and treatment of glaucoma with field loss. In addition it is important to concentrate particular attention on patients belonging to the age group of 60-70 this group being most liable to develop glaucomatous field loss.

Summary

In the present paper an account is given of the results of a follow up carried out five years after routine tonometry among 1882 patients aged over 35 years in ophthalmic practice.

The investigation comprised 169 patients with a pressure value of 20 mm Hg or higher, 10 who also were suspected of glaucoma and finally 538 with pressure values below 20 mm Hg who reconsulted the ophthalmologist within the observation period.

Of the group of 169 patients 110 (65 per cent) were subjected to follow up examination, 46 had died within the observation period and 13 could not be followed up for different reasons.

The assessment of this group with ocular hypertension was based mainly on the 110 patients followed up. The criteria chosen effected that 50 patients were characterized as suffering from glaucoma but only seven with fairly extensive field loss while 48 were characterized as borderline cases and 12 as normal.

Of 54 untreated patients none developed glaucomatous field loss during the

diathermy - retained 3 days - exhibited no trace of moisture. It was believed that the falling tension revealed by the tension measurements could be explained only by internal leakage. Such an internal fistula had to be located in the small iridencleissis region and therefore 16/4 a plastic plomb was applied over this region

A radially situated silicone plomb was attached with sutures in the conjunctiva and anchored in the sclera with the plomb outside the conjunctiva (Fig 1) After application of these sutures it was noted that the tension dropped sharply so that the bulb seemed almost collapsed. However the same evening the bulb had resumed its normal shape and the next morning the anterior chamber had normal depth $T = 15/5.5$

After 48 hours the choroidal detachment persisted only nasally and temporally. After 3 days the choroidal detachment had disappeared after 5 days the plomb was removed

9.4 flushing at the site of the plomb. Fluorescein test negative
 $14/5 V = 5/10 (\pm 0)$ Diffuse bleb at 12 o'clock. Ophthalmoscopy and visual fields as before operation $T \text{ appl} = 10$

In this case a variety of facts indicate that the operative intervention had not induced an external fistula. Normal healing commenced and the conjunctival sutures were removed after 15 days. The tension was 10/5.5 and a bleb was present over the iridencleissis region. A fortnight later however the bleb had disappeared and the tension dropped to 15/5.5 and simultaneously incipient choroidal detachment was noted. Moreover after subsequent psychrodiathermy over the operative field the patient wore bandages for 3 days. When these were changed no signs of moisture were observed.

Assuming that no external fistula was present the rapid fall in tension observed at tonometry according to Schiotz and the disappearance of the symp



Fig 1

The silicone plomb attached over the iridencleissis region

observation period In three of these the pressure level rose to 25 mm Hg or higher but otherwise no alteration in principle was observed towards a higher pressure level in this group

Among 42 treated patients only 18 per cent of the eyes had the pressure level reduced to below 20 mm Hg while 52 per cent had a pressure level of 22 mm Hg or higher Three patients who had previously been declared normal on the basis of ophthalmoscopy and visual field measurement developed glaucomatous field loss while in the remaining seven patients with progression during the observation period ophthalmoscopic changes presence of central vein thrombosis or a familial predisposition had been recorded on the original screening

Of the 538 patients with a screening value below 20 mm Hg who re consulted the ophthalmologist within the observation period 222 or 13 per cent of the original 1703 normals had their intra ocular pressure measured In four of these the measurement gave a value of 25 mm Hg or higher but without glaucomatous field loss being demonstrated

References

- Anonymous* The miotic life Brit J Ophthal 1964 48 354-356
Arnaly M F A glaucoma survey J Iowa St med Soc 1960 50 501-507
Arnaly M F The Des Moines population study of glaucoma Invest Ophthal 1967 1 618-628
Arnaly M F Ocular pressure and visual fields Arch Ophthal 1969 81 25-40
Aulhorn E & H Harms Early visual field defects in glaucoma In Glaucoma symposium Tutzing Castle Basel 1961 p 151-175
Becker B & R N Shaffer Diagnosis and therapy of the glaucomas 2 ed Saint Louis 1965 p 53 & 184-185
Becker B & W R Morton Topical epinephrine in glaucoma suspects Amer J Ophthal 1966 62 272-277
Bertelsen T M Davanger A Kolstad L Wirsching & H Aased Måling av det intra okulære trykk (Schiotz) og spaltelampeundersøkelse av personalet i en større bedrift Tidsskr norske Lægeforen 1965 85 449-453
Chandler P A & W Morton Grant Lectures on glaucoma Philadelphia 1965 p 39 & 116
Dake C L Glaucoma simplex - a long term clinical study Assen 1967 p 16-17
Drance S M V Berry & A Hughes Studies on the effects of age on the central and peripheral isopters of the visual field in normal subjects Amer J Ophthal 1967 63 1661-1672
Frihauf A W Groeschel S Klein & F Muller Glaukom - reiheuntersuchungen 1964/1965/1966 in Dresden Dtsch Gesundh Wes 1968 23 1516-1522
Goldmann H Contribution on discussion on Leydhecker Zur verbreitung des glaucoma simplex in der scheinbar gesunden augenärztlich nicht behandelten bevolkerung Documenta Ophthal 1959 13 382-386
Goldmann H Klinische methoden der untersuchung des intraokularen druckes und der abflussverhältnisse beim primären glaukom Ophthalmologica 1960 139 214-238

toms after application of a silicone plomb suggest that escape of fluid via uveal vessels had taken place in this case. At present nothing can be said as to how common this phenomenon might be.

References

- Chandler P A & Maumenee A E* A major cause of hypotony. *Trans Amer Acad Ophthal Otolaryng* 65: 563 1961
- Dobice J H* The nature of choroidal detachment fluid. *Trans Ophthal Soc U K* 81: 113 1961
- Fuchs E* Ablosung der Aderhaut nach Staroperationen. *Graefes Arch Ophthal* 51: 199 1900
- Fuchs E* Ablosung der Aderhaut nach Operation. *Graefes Arch Ophthal* 53: 375 1902
- Hagen S* Die seröse postoperative Chorioidalablosung und ihre Pathogenese. *Klin Mbl Augenheilk* 66: 161 1921
- Meller J* Über postoperative und spontane Chorioidalahebung. *Graefes Arch Ophthal* 80: 170 1911

Authors address

Professor H Rosengren Fridkullagatan 25 A 412 62 Göteborg Sweden

- Goldmann H Summary in Glaucoma symposium Tutzing Castle Basel 1967 p 256-60
- Graham P. Contribution to the ophthalmological Society of the United Kingdom 83 annual congress 1963 *Brit. J Ophthal* 1963 57 647
- Hoor J S Surgical treatment of open angle glaucoma In symposium on glaucoma Saint Louis 1967 p 175-186
- Louet B Den medikamentelle behandling af primær glaukom *Ugeskr Læg* 1960 122 1 07-106
- Leopold I H Glaucoma masque *Amer J Ophthal* 1967 63 14-178
- Leopold I H Diagnostic criteria for glaucoma and indications for treatment *Highlights Ophthal* 1969 11 03-210
- Leydhecker W Zur verbreitung des glaucoma simplex in der scheinbar gesunden augenärztlich nicht behandelten bevölkerung *Documenta Ophthal* 1959 13 559-560
- Leydhecker W Glaukom - ein handbuch Berlin 1960a p 33-37
- Leydhecker W Die prognose des glaucoma simplex bei behandlung mit miotika im fruhstadium *Klin Mbl Augenheilk* 1960b 137 606-612
- Leydhecker W Die entscheidung zwischen medikamentöser oder operativen therapie bei glaukom *Klin Mbl Augenheilk* 1963 142 760-766
- Leydhecker W Die zuverlässigkeit der diagnose des glaucoma simplex im fruhstadium *Documenta Ophthal* 1966 20 214-229
- Linnar E & U Stromberg The course of untreated ocular hypertension *Acta Ophthal* 1964 42 836-848
- Linnar E & U Stromberg Ocular hypertension - a five year study of the total population in a Swedish town Skövde In *Glaucoma symposium Tutzing Castle* Basel 1967 p 181-194
- Norik K Routine tonometry for detection of glaucoma in patients with a five year follow up *Acta Ophthal* 1967 45 536-545
- Norik K Primary glaucoma as a cause of blindness *Acta Ophthal* 1968 46 853-859
- Norikov A Glaucoma screening - 2 A five year follow up carried through in relation to a glaucoma screening among members of the Volunteer Donor Corps of the island of Falster (Denmark) *Acta Ophthal* 1970a 48 418-433
- Norikov A Routine tonometry in ophthalmic practice - 1 Primary screening and further examinations for diagnostic purposes *Acta Ophthal* 1970b 48
- Pollack I P Diagnosis of the glaucomas In symposium on glaucoma Saint Louis 1967 p 31-61
- Schmidt Th Zur fruhdiagnose und uberwachung des einfachen glaukoma *Ophthalmologica* 1960 139 96-100
- Shaffer R V The miotics In symposium on glaucoma Saint Louis 1967 p 129-131
- Snyder D Glaucoma *Amer J Ophthal* 1969 67 599-600
- Stromberg U Ocular hypertension Thesis *Acta Ophthal suppl* 69 Kbh 1967 p 52
- Su H S Some problems in the management of adult primary glaucomas *Annals of Ophthalmology* 1969 1 73-83
- Tauber E Therapeutic results in primary glaucoma *Acta Ophthal suppl* 61 Kbh 1967 p 40
- Walker H W Some problems in the medical treatment of glaucoma In L B Hunt ed *Glaucoma* London 1966 p 38-10
- Walker R C Lesione C L Gougnard La genese des deficits fonctionnels dans l'œil hypertendu *Documenta Ophthal* 1959 13 751-753
- World Health Organization *Rapp ép dém démogr* 1966 19 2 433-510

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FOUR FAMILIES WITH THE DOMINANT INFANTILE FORM OF OPTIC NERVE ATROPHY

BY

C. C. KOK van ALPHEN

History

In the last eight years there has been much more interest in hereditary optic nerve atrophy especially in the infantile forms.

The former confusion between the Leber type and the dominant and recessive infantile forms now belongs to the past. In the following survey of the literature of the last eight years we exclude publications about the Leber form of optic atrophy as well as publications about that group of hereditary optic atrophies which are associated with cerebral or other neurological disturbances (the Behr form etc.).

François *et al.* published in 1960 a comparative study of acquired colour vision defects associated with the different types of hereditary optic atrophy. In the Leber type he found red-green defects; in the dominant infantile form blue-green defects.

Marschall *et al.* (1963) described a family with two sisters with the typical picture of the dominant infantile form of optic atrophy (DIOA). Two children of these sisters showed the typical form; two were dubious cases with temporal pallor of the optic disc and quite good vision; three children were unaffected.

Ferdinando (1963) described a family with DIOA. He did not mention colour defects in this family.

Cornet (1963) published a family with DIOA combined with deafness.

Cruickshank (1963) described a pedigree with 55 cases. In three of these the disease started between the second and third year. Four cases showed function

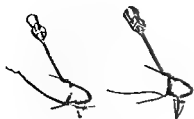


Fig 5



Fig 6

structed section is more extensive but the patent part of the canaliculus adjoining the sac reaches to the lacrimal lacus an artificial lacrimal punctum is formed by a trephine above the tip of the inserted retrograd cannula (Fig 6) It should be mentioned here that the X ray contrast medium pumped through the intact canaliculus or if both canaliculi are obstructed percutaneously into the lacrimal sac hardly ever reaches up to the obstruction Therefore it is problematic to determine by X ray the exact site of the obstructed section of the canaliculus

In cases of obstructed canaliculi - of course - also we attempt probing too For better and more prolonged dilatation of the obstructed canaliculus Hyaluronate and own blood serum is added to the anaesthetic solution injected into the scarred area Then we fill up the canaliculus with cysteine solution to promote epithelisation Our results are encouraging but rarely lasting in more extensive obstructions

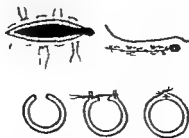


Fig 7

stump of the lacerated canaliculus too and the rupture is united in the usual manner

To employ the retrograd cannula seems preferable to the other retrograde procedures (5 6 7 8 9 10 11 12) as it is quite easily introduced following the simultaneous syringing and as the thread is driven within the canule the canicular epithelium is not exposed to further damage

If the lacerated canaliculus can't be approached even from the intact one or if both canaliculi are lacerated or obstructed the retrograde procedure must be performed from the incised sac

The retrograde procedure enables us also to gauge the length of the obstructed part of the canaliculus. The impassable part can be flanked by the retrograd cannula from the sac and by a Bowman's probe from the lacrimal punctum (Fig 5). A few mm's of the canaliculus may then well be excised and the two stumps - round a plastic thread - united perfectly end to end. If the ob-

Fig 3

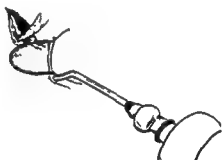


Fig 4



Fig 1

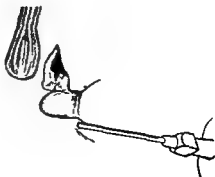


Fig 2



nal defects but no ophthalmological abnormalities. He found blue-colour defects and in some cases abnormal dark adaptation.

Klein (1964) discussed a symposium on hereditary optic atrophies.

Rivara (1964) examined by static perimetry the fields of vision in three cases in a family with DIOA who had a fairly good visual acuity (0.4-0.5). He found enlargement of the blind spots and a limitation of the peripheral fields.

Rose (1964) gave a useful description of the various ways in which optic atrophy can be classified.

Schwartz (1964) described 48 children with optic atrophy without evidence of diffuse cerebral or systemic disease but no information about the heredity is given.

Bergamini (1964) mentioned a family with congenital optic atrophy with ptosis, aniridia, cataract and nystagmus.

Proto (1965) published a family with DIOA in which especially women were affected.

Kozousek (1965) reported a dominant hereditary optic nerve atrophy approaching Kjer's form with asymmetry of the face, dental anomalies, deformation of the ears and the tongue and lowered intelligence.

François (1966) published a very informative paper. Congenital or infantile optic atrophy of autosomal recessive heredity is rare.

Jaeger & Grulner (1966) described the changes in the colour sense in familial macular degeneration and in hereditary optic atrophies. Patients with macular diseases show anomalies in colour sense for red-green; patients with DIOA anomalous blue vision.

Grulner (1966) examined members of four pedigrees with DIOA for haemoglobin components of the serum and also for the various blood groups. There was no indication that there was a genetic linkage between these haematological conditions and the ocular manifestations. In addition there was no evidence to suggest a linkage between this inherited form of optic atrophy and the inherited low voltage EEG which was found incidentally.

Jaeger (1966) emphasizes that the differential diagnosis of the hereditary optic atrophies in childhood is of great importance with regard to prognosis. Patients with DIOA can mostly be trained in a normal school and later on can support their families but patients with the congenital dominant or recessive form must follow an occupation for the blind or at the best for the partially sighted.

Hellner & Haase (1967) performed electroretinographic studies in two families with DIOA. Disorders of the photopic ERG were observed. Lower photopic potentials and reduced maximal flicker fusion frequencies were characteristic.

The increment threshold determined electroretinographically in increasing light adaptation demonstrates a lowered general sensitivity of the retina compared with a normal control group.

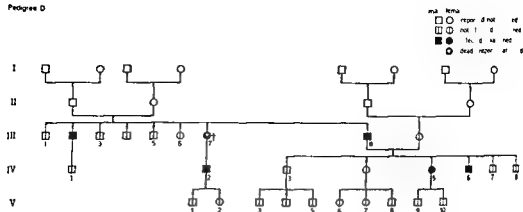


Fig 4
Pedigree D

Discussion

Time of onset of the disease

In all four pedigrees the time of onset was in the early years of childhood generally between 3 and 10 years of age the youngest affected child known was 1 year old

In our material the disease has not yet been demonstrated at birth which fact seems to exclude the congenital form A few cases of nystagmus were however noted in pedigree A

Abnormalities of the fundus

Optic nerve atrophy was found in all four pedigrees In pedigree A B and D no dubious cases existed On the other hand pedigree C showed cases with normal fundi and poor vision and vice versa In pedigree D the papillae were totally white with no difference between the temporal and nasal sides

Visual acuity

In the serious cases of pedigree A B and D vision was less than 0.1 in the slighter cases 0.2-0.5

In pedigree C no serious cases were found

Refraction

In all affected members of the four pedigrees myopia was found

Rorsman (1967) and Rose (1966) describe optic atrophy combined with diabetes mellitus in children of 14-18 years of age

Smolin (1961) reported one family with DIOA

Wilson (1967) reports in a paper on several forms of optic atrophy. Patients with DIOA in whom the disease occurs at an earlier age have a worse visual prognosis

Virshup (1968) emphasizes again the three forms of hereditary optic atrophy: the DIOA, the congenital or infantile recessive form and the Leber type

Present investigation

Our own investigation concerns four Dutch pedigrees with DIOA. Thanks to the Netherlands General Association for Prevention of Blindness, fieldworkers of this Association did much work in determining the family relationships and in investigating many members of the families scattered throughout the Netherlands

Pedigree A

The first pedigree about which I published a paper in 1960 was totally re-investigated in 1967-1968. The affected members did not seem worse than in 1960. The younger affected children of family VI 8-20 showed a slight increase in myopia. Visual acuity with correction however did not diminish. There were still no signs of optic atrophy in the body VI 19 who seemed unaffected in 1960. However one more girl (VI 20) had been born in this family and I could follow this child closely myself. At the age of two years, though a distinctive pallor of the temporal part of the disk was seen, the girl seemed to have a normal visual acuity for her age. Now at the age of six the vision is OD 0.2 OS 0.3 and she shows clearly a red-green colour defect. She shows no strabismus as yet. Probably the disease was not congenital. I have seen this child many times since birth. The colour vision of this large family was tested again with the HRR test but no blue-yellow defects were noted. The family VI (8-20) living in Leyden could be examined by myself at will. The affected children showed red-green defects at the age of 4-6 years as soon as they could be examined for colour vision.

As I noted in my previous paper, the expression of the diseases in this family is very variable. The younger generation is definitely less seriously affected than the earlier ones. However the identical twins (VI 48 and 49) are socially blind and have had to attend a school for the blind. Nystagmus was only noted

Strabismus

In pedigree A and II we found strabismus divergens in all affected members
In pedigree C and III no strabismus has been seen

Visual fields

Wedge formed peripheral defects already described in 1960 were found in some members of pedigree A

The affected members of pedigrees B C and D had in general no peripheral defects only III 38 showed slight concentric limitation All affected members of the four pedigrees showed enlargement of the blind spot and/or paracentral scotomata

Colour sense

Pedigree A was again investigated with the HRR test The serious cases had achromatopsia the slighter cases distinct red green defects In pedigree B also we found achromatopsia in the serious cases in the slight cases some red green defects definitely no blue defect. On the contrary some members of pedigree C showed slight blue defects Some cases in pedigree II showed red green as well as blue yellow defects When comparing these pedigrees with other extensively investigated pedigrees (Jaeger Grutzner Kjer etc) it is notable that pedigrees A and B definitely show no typical disturbance of blue yellow perception on the other hand pedigree B shows a definite defect in red green colour vision Pedigree C shows a slight disturbance in the blue in a few cases colour vision being more often normal in the affected sibs of this family

Pedigree D is exceptional in having both colour vision defects

A comparison of the above mentioned symptoms in the four pedigrees is made in table I

Nystagmus

This symptom was only observed in pedigree A in three of the most serious cases (V 4 V 13 V 15)

Electroretinography

Except in some very serious cases no abnormalities were found in pedigrees A B and C No E.R.G.s are available from pedigree D

No other physical or neurological anomalies were found

Heredity

The pedigrees A and B are in agreement with the rules for dominant autosomal

Postscript A

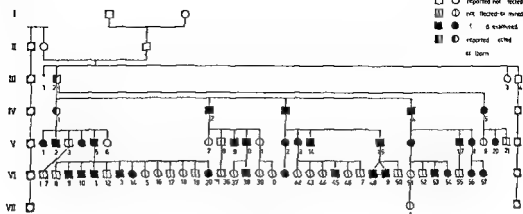


Fig 1
Pedigree A

in three cases (V 4 V 13 V 15) No new cases were found with the exception of VI 20 The two eldest affected sons of the Leyden family (V 19 and VI 10) are engaged to be married and it will be interesting to see the development of their children later on However some members of the family have purposely adopted children so we will not be able to follow the affection in their offspring

Pedigree B

The members of this pedigree were for the most part examined at the Eye Hospital in Rotterdam all the families live in the neighborhood of this town. Much work was done on this pedigree of which only a small part proved to be affected. The members who show the disease resemble closely the affected members of pedigree A.

The older generation is more seriously affected than the younger wone with visual acuity less than 0.1 some of them show strabismus divergens (VI 87 and 89) In generation V again myopia occurs The girl V 134 was quite normal up to her 12th year then her visual acuity deteriorated to 0.5 the disks showing an increasing temporal pallor A follow up of the fundus by colour photography was made The ERG was normal the Bjerrum showed somewhat enlarged blind spots

The boys V 142 and V 143 were affected at a somewhat younger age V 142 had obvious signs of pallor of the disks and visual acuity ODS 0.3 at the age of 10 years V 143 had visual acuity ODS 0.3 at the age of 7 years

They both deteriorated to a vision of ODS 5/60 II and although they had

Table 1

	Vision		Reflected		Colour
	S o s c o s	L i g h t c o s	S t b m s	V s a l f e l d s	
<u>Ped g ee A</u>	< 0.1	0.2 0.5	myop a d e g e t t b s m	wedge shaped defects m a c e t a l scotom e	d f e c t e d g e
<u>P d g ee B</u>	< 0.1	0.2 0.5	my p d e g f s t a b m u s	p a c e n t a l o t m a t	b l e d f e c t s
<u>P d g ee C</u>	n o s e n u s	0.2 1 d b t c a s	my p n o t a b s m u s	p a c e n t a l s c o t o m a t e	d b o s b l e d f e c t s
<u>Ped g D</u>	< 0.1	0.25	myop a o s t a b m u s	p a c e t l o t o m e	d f e c t s n e d g + b l e y e l l o w

heredity Both pedigrees show affected members in more than two generations. The ratio of affected to healthy individuals (theoretically 1:1) is in pedigree A for the 14 sibships of the generations IV-V and VI - all offspring of affected parents - 34:24 in pedigree B for the four sibships of the generations IV and V 7:8.

The pedigrees C and D differ from A and B in that they as yet only show affected members in two generations and in that in the first affected generation three diseased sibs have appeared. This could suggest recessivity but the fact that in both pedigrees the offspring of the affected parent include several affected children is more suggestive of dominance. In the pedigrees A, B and D X-chromosomal heredity can be excluded by heredity from father to son. The fact that in pedigree C women and men are equally affected also argues X-chromosomal heredity.

In pedigree A in particular the expression is very variable.

In none of the pedigrees does the disease skip a generation.

The mutation can probably be found in

Pedigree A III-2

Pedigree B III-28

Pedigree C } unknown because in the first affected generation three members

Pedigree D } show the disease

Summary

Two pedigrees with a dominant infantile form of optic atrophy and two pedigrees with a probably dominant infantile form of optic atrophy are described.

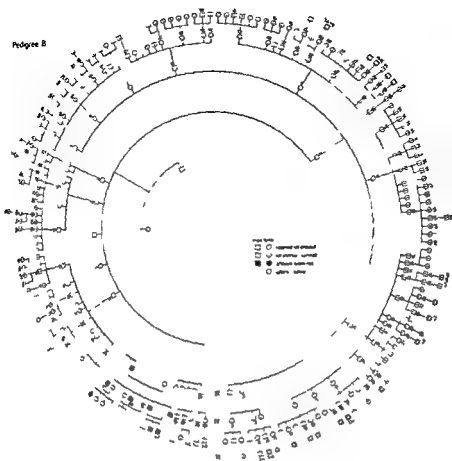


Fig 2
Pedigree II

normal peripheral fields of vision they had to be trained in a school for the blind

As to the colour vision blue green defects were definitely not observed. In the serious cases it was not possible to do colour investigations. In the other members no colour defects or only very slight green red defects were found. ERG's and dark adaptation curves were normal, the latter in the more serious cases somewhat too high.

A very interesting fact is that patient IV 89, who is seriously affected married by second marriage a woman known to have Leber's optic atrophy. She figures in a pedigree of Waardenburg and in one of van Senus. Out of this

The disease develops during childhood. The expression of the disease is variable. vision 0 0 2 0 5

The abnormalities in the fundus are very typical: pale disks, most often whiter on the temporal side.

In most cases the visual fields are peripherally normal. In some cases in pedigree A wedge formed peripheral defects were found and in one case in pedigree C a slight concentric limitation. In all affected cases there are enlarged blind spots or paracentral scotomata.

In the serious cases achromatopsia is found. The slighter cases in pedigrees A and U show a definite disturbance in red green vision. In pedigree C however some sibs show defects in the blue. Pedigree IV shows blue yellow as well as red green defects. Electroretinography gives fairly normal results.

Because of the good peripheral fields of vision all the less seriously affected individuals can maintain themselves in the community.

As far as we can determine the disease is not congenital. It is however of importance to examine the new born children as early as possible. When making a differential diagnosis in a case of optic nerve atrophy the general ophthalmologist must be aware of the existence of this affection.

Several neurosurgical operations and needless neurological investigations could have been spared if some time had been given to a simple investigation of the patient's family.

References

- Bergamini L, Ferraris F et al. A singular association of familial congenital neuro-ophthalmological syndromes (ptosis, aniridia, cataract, nystagmus, optic atrophy). *Acta neurol (Napoli)* 1964; 19: 6-10, 17.
- Ferdinando II di. Atrofia ottica ereditaria a carattere dominante (Hereditary Opticus atrophy mit dominantem Vererbungscharakter). *Riv oto-neuro-oftal* 38: 28, 10, 1964.
- François J, Verriest G, François P et al. Comparative study of acquired colour vision defects associated with the different types of hereditary optic atrophy. *Bull Soc Belge Ophthal* 193: 950-956, 1960.
- François J. Mode d'hérédité des hérédo-dégénérescences du nerf optique. *J Genet hum* 1966; 15: 3-4, 147-221.
- Gernet H. Hereditäre Opticusatrophie in Kombination mit Taubheit. Ber über die 62. Zusammenkunft der Dtsch ophthal Ges in Heidelberg vom 24-28 Sept. 1963: 545-54.
- Gritner P. Koppelungsuntersuchungen bei der infantilen dominant vererbten Opticus Atrophie. *Humangenetik* 9: 363-371, 1966.
- Gritner P. Über Diagnose und Funktionsstörungen bei der infantilen dominant vererbten Opticus Atrophie. Bericht über die 65. Zusammenkunft der Dtsch ophthal Ges in Heidelberg vom 24-28 Sept. 1963: 268-273.

Pedagogues A

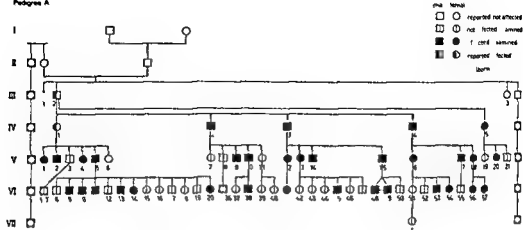


Fig 1
Pedigree A

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- Harcourt B & Jay B Bilateral optic atrophy in childhood Brit J Ophthal vol 51 786 787 1968
- Hellner A A & Haase W Über elektroretinographische Befunde bei der dominanten juvenilen Opticus atrophie Albr von Graefes Arch Ophth Bd 112 159 163 1961
- Jaeger W & Grutner P Changes in the colour sense of familial macular degeneration and in hereditary optic atrophies Bull Oculist 45 83 810 1966
- Jaeger W Hereditary optic atrophies in childhood J Genet hum 1966 15/3 4 319 321
- Kjer P Infantile optic atrophy with dominant mode of inheritance Acta Ophth Suppl 54 1959
- Klein D Las atrofias hereditarias del nervio optico (Die erblichen Opticusatrophien) Rev neurol B Aires 22 93 96 1964
- Lok van Alphen C C A family with the dominant infantile form of optic atrophy Acta Ophthalmologica 38 1960
- Loosch J et al Hereditary optic nerve atrophy approaching Kjer's form Acta fac med univ Brunen 25 171 176 1965
- Marschall M R & Coulas R G Hereditary optic atrophy Trans Canad ophthal Soc 26 86 92 1963
- Michal S et al Atrophie optique heredo familiale dominante associee à la surdimutité Ann oculist Paris 201 431 435 1963
- Proto F On a family affected by hereditary optic atrophy with dominant character Bull Oculist 1965 44/8 592 597
- Rivara A Perimetrische und kampimetrische Untersuchungen an Fällen von begeben heredo familiarer infantiler Opticusatrophie Bull Oculist 43 813 821 1964
- Roisman G & Soderstrom N Optic atrophy and juvenile diabetes mellitus with familial occurrence Acta Med Scand vol 182 419 425 1967
- Rose F C et al The association of juvenile diabetes mellitus and optic atrophy Quart J Med 35 385 405 1966
- Rose F C Optic atrophy Postgrad med j 40 692 695 1964
- Schwartz J F et al Optic atrophy in childhood Pediatrics 34 610 619 1964
- Smolin G Infantile hereditary optic atrophy Amer J Ophthal vol 62 167 164 1967
- Wilson J Optic atrophy in childhood Proc roy Med 60 157 158 1961

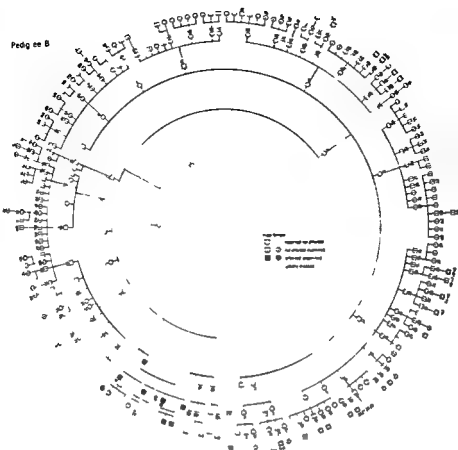


Fig 6
Pedigree B

normal peripheral fields of vision they had to be trained in a school for the blind

As to the colour vision blue green defects were definitely not observed In the serious cases it was not possible to do colour investigations In the other members no colour defects or only very slight green red defects were found E R G s and dark adaptation curves were normal the latter in the more serious cases somewhat too high

A very interesting fact is that patient IV 89 who is seriously affected married by second marriage a woman known to have Leber's optic atrophy She figures in a pedigree of Waardenburg and in one of van Senns Out of this

*Aus der Universitäts Augenklinik Jena
(Direktor Prof Dr med habil A Heydenreich)*

NYKTOMETERUNTERSUCHUNGEN BEI MAKULAERKRANKUNGEN

VON

JOHANNA ORTLEPP

Einleitung

Hin und wieder stehen wir bei unserer augenärztlichen Untersuchung einer Diskrepanz zwischen den Klagen des Patienten über sein schlechtes Sehvermögen und den sehr guten subjektiven Visusangaben bei der Prüfung an unseren Sehprobentafeln gegenüber. Die Ursache ist in Folgendem zu suchen.

Wir berücksichtigen bei der üblichen Sehscharfeproofung nicht die Zeit die zur Erkennung eines Sehzeichens benötigt wird. Die Sehscharfeproofung findet bei gunstiger Beleuchtung statt. Sehzeichen und Grund weisen einen starken Kontrast auf. Bei den vielfältigen taglichen Anforderungen aber die an die Sinnesleistung des Auges unseres Patienten gestellt werden spürt der Patient sein Unvermögen, denn hier liegen oft nicht so gunstige Leuchtdichtebedingungen vor wie bei unserer Visus Prüfung.

Wir haben bei Patienten mit guter Sehscharfe aber feinen makularen Veränderungen am Registrier Nyktometer des VEB Carl Zeiss Jena das auf das Nyktometer von COMBERC zurückgeht Sofortadaptation und Blendempfindlichkeit untersucht mit der Fragestellung:

Liegen die Prüfungsergebnisse im Normbereich wie er für die verschiedenen Altersgruppen gefunden wurde?

Gibt uns das Registrier Nyktometer eine bessere Information über die Funktion bei Makulaerkrankungen als die übliche Visusprüfung?

Eingegangen am 3. Dezember 1969

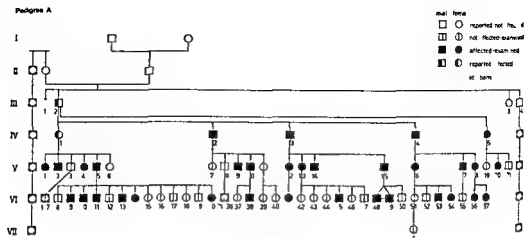


Fig 1
Pedigree A

in three cases (V 4 V 13 V 15) No new cases were found with the exception of VI 20 The two eldest affected sons of the Leyden family (V 19 and VI 10) are engaged to be married and it will be interesting to see the development of their children later on However some members of the family have purposely adopted children so we will not be able to follow the affection in their offspring

Pedigree B

The members of this pedigree were for the most part examined at the Eye Hospital in Rotterdam all the families live in the neighborhood of this town Much work was done on this pedigree of which only a small part proved to be affected The members who show the disease resemble closely the affected members of pedigree A

The older generation is more seriously affected than the younger wone with visual acuity less than 0.1 some of them show strabismus divergens (VI 87 and 89) In generation V again myopia occurs The girl V 134 was quite normal up to her 12th year then her visual acuity deteriorated to 0.5 the disks showing an increasing temporal pallor A follow up of the fundus by colour photography was made The ERG was normal the Bjerrum showed somewhat enlarged blind spots

The boys V 142 and V 143 were affected at a somewhat younger age V 142 had obvious signs of pallor of the disks and visual acuity ODS 0.3 at the age of 10 years V 143 had visual acuity ODS 0.3 at the age of 7 years

They both deteriorated to a vision of ODS 5/60 0.1 and although they had

- Harcourt B & Jay B* Bilateral optic atrophy in childhood *Brit J Ophthal* vol 59 786 787 1968
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- Jaeger W & Grutner P* Changes in the colour sense of familial macular degeneration and in hereditary optic atrophies *Bull Oculist* 45 783 810 1966
- Jaeger W* Hereditary optic atrophies in childhood *J Genet hum* 1966 15/3 4 317 321
- Kjer P* Infantile optic atrophy with dominant mode of inheritance *Acta Ophth Suppl* 54 1959
- Klein D* Las atrofias hereditarias del nervio optico (Die erblichen Opticusatrophien) *Rev neurol B Aires* 22 93 96 1964
- Kok van Alphen C C* A family with the dominant infantile form of optic atrophy *Acta Ophthalmologica* 38 1960
- Kousck J et al* Hereditary optic nerve atrophy approaching Kjer's form *Acta fac med univ Brunen* 25 171 176 1965
- Marschall M R & Coulas R G* Hereditary optic atrophy *Trans Canad ophthal Soc* 26 86 92 1963
- Michal S et al* Atrophie optique heredo familiale dominante associee a la surditte. *Ann oculist Paris* 201 431 435 1963
- Proto F* On a family affected by hereditary optic atrophy with dominant character *Bull Oculist* 1965 44/8 592 597
- Rivara A* Perimetrische und kampimetrische Untersuchungen an Fallen von beegenn heredo familiarer infantiler Opticusatrophie *Bull Oculist* 43 815 821 1964
- Rorsman G & Soderstrom N* Optic atrophy and juvenile diabetes mellitus with familial occurrence *Acta Med Scand* vol 182 419 425 1967
- Rose F C et al* The association of juvenile diabetes mellitus and optic atrophy *Quart J Med* 35 385 405 1966
- Rose F C* Optic atrophy *Postgrad med j* 40 692 695 1964
- Schwartz J F et al* Optic atrophy in childhood *Pediatrics* 34 670 679 1964
- Smolin G* Infantile hereditary optic atrophy *Amer J Ophthal* vol 62 167 164 1967
- Wilson J* Optic atrophy in childhood *Proc roy Med* 60 157 158 1967

them were unable to see any of the H R R plates Generation IV had two affected and six dubious cases As to the dubious cases

IV 23 has normal vision temporal pallor of the disks and only 5 capillaries

IV 35 has normal visual acuity (Vis ODS with $s-2 =$) but a definite pallor of both papillae

IV 34 has poor vision (Vis ODS with $s-1 = 0.25$) but no visible pallor of the papillae.

IV 36 has slight pallor of both disks and a visual acuity of ODS 0.3

IV 38 has normal vision slight temporal pallor of the papillae and some concentric narrowing of the peripheral fields of vision

IV 39 is like IV 23 Vis ODS 1 temporal pallor of the disks 6 small vessels counted

Visual fields were generally normal peripherally (except IV 38) The definitely affected members showed paracentral scotomata

Some of the less affected and dubious cases showed a dubious blue defect definitely no red green defect the more serious cases could not name any colour

A further investigation into the colour vision of this pedigree is still going on at the Utrecht Hospital and will be published later

One patient (III 11) underwent many needless examinations by neurologists and other specialists because no diagnosis of her condition could be made Needless to say how much time and trouble could have been spared by a better anamnestic investigation of the family

Pedigree II

Because the members of this pedigree are living to the North of Amsterdam they were investigated at the University Eye Clinic of that town

The fundi resemble those of the affected members of the first three pedigrees They all show pale papillae but in the members of this pedigree all disks are totally white

The periphery of the visual field is normal but the blind spots are enlarged The affected members of this pedigree have defects of colour vision both red green and blue yellow

Case IV 6 shows defects of red green as well as yellow blue vision.

Case IV 5 shows defects in red green and blue A further investigation of these rare symptoms is still proceeding in the Amsterdam Hospital and will be published in due course)

In the most serious cases investigation of the colour vision was impossible (III 2 and 8 IV 2)

Case III 1 was deceased at the time of the investigation but reported affected

ration wurden + 40 und + 50 D sphärisch gebraucht auch bei Retinitis centralis serosa einmal + 40 D sphärisch

Die Untersuchung erfolgte monokular einmalig bei nicht erweiterter Pupille. Eine weitere Untersuchung mit Minusgläsern diente zum Ausschluss einer Nachtmyopie. In den vorliegenden Fällen konnte keine solche nachgewiesen werden.

Bei den Verlaufsuntersuchungen der Retinitis centralis serosa war bei einigen wenigen Untersuchungen die Pupille erweitert. In diesen Fällen wurde die Helladaptation am Gerät stenopäisch vorgenommen, um eine nachhaltige Blendung zu verhindern. Der Vergleich mit den zuvor und danach bei enger Pupille erhaltenen Ergebnisse gestattete uns, die so gewonnenen Untersuchungsergebnisse mit in die Tabelle aufzunehmen. Der Patient wurde zu schnellen Angaben am Nyktometer angespornt. Eine Zeile galt als richtig gelesen, wenn von den 5 angebotenen Zahlen 4 richtig erkannt wurden.

Das Untersuchungsprogramm des Registrier-Nyktometers des VEB Carl Zeiss Jena läuft automatisch folgendermassen ab. Es beginnt mit einer 3 Minuten langen Helladaptation an 1000 asb. Daran schliesst sich die Sofortadaptation von 2 Minuten Dauer an, wobei eine Fernvisusprüfung vorgenommen wird. Die Sehprobentafel besitzt jetzt eine Leuchtdichte von 0,5 asb. Optotypen der Zahlenkombinationen 1 4 1 0 finden sich auf der Tafel, die einen Visus von 0,1 bis 1,0 entsprechen. Darauf folgt die Prüfung der Blendempfindlichkeit. Unter Einwirkung eines Blendlichtes, das die gleiche Blendwirkung hat wie sie im nächtlichen Strassenverkehr angetroffen ist, muss der Prüfling die Zahlentafel lesen. Jeweils nach 27 Sekunden ändert sich die Leuchtdichte der Sehprobentafel. Sie steigt von 0,5 asb auf 4 und auf 32 asb.

Ergebnisse

Sofortadaptation

Von unseren 46 geprüften Augen erreichten 19 am Nyktometer keine Schärfe, die Sofortadaptation war völlig aufgehoben (Tab. 2). 9 dieser Augen hatten eine Schärfe von 5/4 an der Sehprobentafel, 12 erlangten einen Visus von 0,1 und 11 einen von 0,2 im Verlauf der Sofortadaptation (Tab. 2).

Diese Werte liegen bei Berücksichtigung des Alters, das bei der Beurteilung der Sofortadaptation und Blendempfindlichkeit nach Braun, Heimius, Schober, Aulhorn und Harms, Sachs, Lehnert und Schmidt wesentlich ist, nicht mehr in derhalb des normalen Streubereiches.*

4 Augen liegen mit einem Visus von 0,3 am Nyktometer noch im unteren

Für die Aufstellung der altersabhängigen Normalwerte am Registrier-Nyktometer des VEB Carl Zeiss Jena danke ich Fraulein cand. med. G. Geyer.

marriage one daughter was born who is - up to now - quite normal The two daughters from the first marriage of IV 89 are normal too (V 138 and 139)

The investigation of heredity in cases of optic atrophy is of great importance This is for instance proved by the fact that member IV 91 was diagnosed as a case of Leber's optic atrophy and as such was operated upon by a neuro surgeon Of course this still rather dangerous operation has been without success The same fate overcame one of the members of pedigree A patient V 20 She too was operated on as a case of Leber's optic atrophy by another neuro surgeon in another town

If hereditary investigation had been done earlier these two patients would have been spared a useless operation

Pedigree B

As the members of this pedigree are living in the eastern provinces and in the new Zuiderzee diked provinces they were investigated as the Ooglijders Gasthuis in Utrecht

This pedigree differs from the first two It shows in addition to evidently affected members dubious cases as in the family described by Marshall In the third generation the patients 7, 10 and 11 have the fully developed disease although their visual acuity is fair (0.2-0.5) Their fundi show temporal pallor of the disc An investigation counting the small capillaries on the papilla was made in this family Instead of the 8-9 capillaries seen on the normal papilla only 3-5 were found in these three patients It is remarkable that all three of

Pedigree C

male female
 □ ○ reprobated not affected
 ▢ ♂ not affected married
 ■ ● affected married
 ⊠ ⊗ dubious

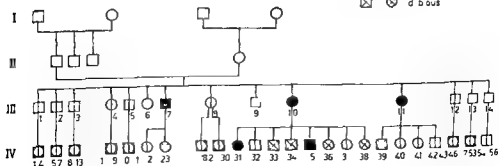


Fig. 5
Pedigree C

Weiterhin wurden einige Patienten mit Retinitis zentralis serosa wiederholt während ihrer Erkrankung am Registrier-Nyktometer geprüft, um festzustellen wie sich Sofortadaptation und Blendempfindlichkeit während des Krankheitsverlaufes verhalten

Methodik

46 Augen an 36 Patienten der Universitäts Augenklinik Jena wurden am Registrier Nyktometer des VEB Carl Zeiss Jena untersucht. Davon wurden in 4 Fällen von Retinitis zentralis serosa mehrmalige Untersuchungen in einem Fall bis zu 14 während der Erkrankung vorgenommen. In den übrigen Fällen handelte es sich um verschiedene Erkrankungen (s. Tab. 1). Abgesehen von den Makuladegenerationen und der Retinitis zentralis serosa galten die makularen Veränderungen aufgrund des ophthalmoskopischen Befundes als nicht mehr frisch sondern wurden als vernarbt angesehen.

Altersmäßig war unsere Patientengruppe ganz heterogen zusammengesetzt. Die jüngsten Patienten waren 15, die ältesten 56 Jahre alt. Nur 4 Patienten waren über 50 Jahre alt. 19 Patienten waren jünger als 40 Jahre.

Die brechenden Medien waren in allen Fällen klar.

An der Sehprobentafel betrug die Sehschärfe $\frac{3}{4}$ $\frac{5}{5}$ $\frac{5}{7}$. Die Nyktometerprüfung wurde mit Fernkorrektur durchgeführt. Die Refraktionen lagen im Bereich von $+2.5$ bis -2.0 D sphärisch. Jedoch in einem Fall von Makuladegene-

Tabel 1
Makulaerkrankungen

Erkrankung der untersuchten Augen	Anzahl d. Augen
Retinitis zentralis serosa	10
Chorioretinitis paracentralis	6
Chorioretinitis disseminata	10
Iridocyclitis mit Makulaveränderungen	5
Periphlebitis mit Makulaveränderungen	2
Chorioretinitis juxtapapillaris	1
Makuladegeneration	12
	insges. 46

them were unable to see any of the HRR plates Generation IV had two affected and six dubious cases As to the dubious cases

IV 23 has normal vision temporal pallor of the disks and only 3 capillaries

IV 30 has normal visual acuity (Vis ODS with s-2 =) but a definite pallor of both papillae

IV 34 has poor vision (Vis ODS with s-1 = 0.25) but no visible pallor of the papillae

IV 36 has slight pallor of both disks and a visual acuity of ODS 0.3

IV 38 has normal vision slight temporal pallor of the papillae and some concentric narrowing of the peripheral fields of vision

IV 39 is like IV 23 Vis ODS 1 temporal pallor of the disks 6 small vessels counted

Visual fields were generally normal peripherally (except IV 38) The definitely affected members showed paracentral scotomata

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A further investigation into the colour vision of this pedigree is still going on at the Utrecht Hospital and will be published later

One patient (III 11) underwent many needless examinations by neurologists and other specialists because no diagnosis of her condition could be made Needless to say how much time and trouble could have been spared by a better anamnestic investigation of the family

Pedigree D

Because the members of this pedigree are living to the North of Amsterdam they were investigated at the University Eye Clinic of that town

The fundi resemble those of the affected members of the first three pedigrees They all show pale papillae but in the members of this pedigree all disks are totally white

The periphery of the visual field is normal but the blind spots are enlarged The affected members of this pedigree have defects of colour vision both red green and blue yellow

Case IV 6 shows defects of red green as well as yellow blue vision

Case IV 5 shows defects in red green and blue A further investigation of these rare symptoms is still proceeding in the Amsterdam Hospital and will be published (due course)

In the most serious cases investigation of the colour vision was impossible (III 2 and 8 IV 2)

Case III 7 was deceased at the time of the investigation but reported affected

ration wurden $+40$ und $+50$ D sphärisch gebraucht auch bei Retinitis centralis serosa einmal $+40$ D sphärisch

Die Untersuchung erfolgte monokular einmalig bei nicht erweiterter Pupille Eine weitere Untersuchung mit Minusgläsern diente zum Ausschluss einer Nachtmyopie In den vorliegenden Fällen konnte keine solche nachgewiesen werden

Bei den Verlaufsuntersuchungen der Retinitis centralis serosa war bei einigen wenigen Untersuchungen die Pupille erweitert In diesen Fällen wurde die Helladaptation am Gerät stenopaisch vorgenommen um eine nachhaltige Blendung zu verhindern Der Vergleich mit den zuvor und danach bei enger Pupille erhaltenen Ergebnisse gestattete uns die so gewonnenen Untersuchungsergebnisse mit in die Tabelle aufzunehmen Der Patient wurde zu schnellen Angaben am Nyktometer angespornt Eine Zeile galt als richtig gelesen wenn von den 5 angebotenen Zahlen 4 richtig erkannt wurden

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Ergebnisse

Sofortadaptation

Von unseren 16 geprüften Augen erreichten 19 am Nyktometer keine Sehscharfe die Sofortadaptation war völlig aufgehoben (Tab 2) 9 dieser Augen hatten eine Sehscharfe von $5/4$ an der Sehprobentafel 12 erlangten einen Visus von 0.1 und 11 einen von 0.9 im Verlauf der Sofortadaptation (Tab 2)

Diese Werte liegen bei Berücksichtigung des Alters das bei der Beurteilung der Sofortadaptation und Blendempfindlichkeit nach Braun Heinsius Schober Aulhorn und Harms Sachs Lehnert und Schmidt wesentlich ist, nicht mehr in der Nähe des normalen Streubereiches

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Für die Aufstellung der Altersabhängigen Normalwerte am Registrier-Nyktometer des VEB Carl Zeiss Jena danke ich Fraulein cand med G Geyer

stricted section is more extensive but the patent part of the canaliculus adjoining the sac reaches to the lacrimal lacus an artificial lacrimal punctum is formed by a trephine above the tip of the inserted retrograd cannula (Fig 6) It should be mentioned here that the X ray contrast medium pumped through the intact canaliculus or if both canaliculi are obstructed percutaneously into the lacrimal sac hardly ever reaches up to the obstruction Therefore it is problematic to determine by X ray the exact site of the obstructed section of the canaliculus

In cases of obstructed canaliculi - of course - also we attempt probing too for better and more prolonged dilatation of the obstructed canaliculus Hya some and own blood serum is added to the anaesthetic solution injected into the scarred area Then we fill up the canaliculus with cysteine solution to promote epithelisation Our results are encouraging but rarely lasting in more extensive obstructions

Fig 5

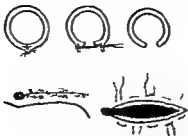


Fig 6



stump of the lacerated canaliculus too and the rupture is united in the usual manner

To employ the retrograd cannula seems preferable to the other retrograde procedures (5 6 7 8 9 10 11 12) as it is quite easily introduced following the simultaneous syringing and as the thread is driven within the canule the canalicular epithelium is not exposed to further damage

If the lacerated canaliculus can't be approached even from the intact one or if both canaliculi are lacerated or obstructed the retrograde procedure must be performed from the incised sac

The retrograde procedure enables us also to gauge the length of the obstructed part of the canaliculus. The impassable part can be flanked by the retrograd cannula from the sac and by a Bowman's probe from the lacrimal punctum (Fig 5) A few mm of the canaliculus may then well be excised and the two stumps - round a plastic thread - united perfect end to end If the ob-

Fig 3

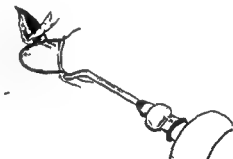


Fig 1

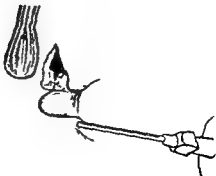


Fig 4



Fig 2



Weiterhin wurden einige Patienten mit Retinitis zentralis serosa wiederholt während ihrer Erkrankung am Registrier Nyktometer geprüft um festzustellen wie sich Sofortadaptation und Blendempfindlichkeit während des Krankheitsverlaufes verhalten

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Altersmäßig war unsere Patientengruppe ganz heterogen zusammengesetzt. Die jüngsten Patienten waren 15 die ältesten 56 Jahre alt. Nur 4 Patienten waren über 50 Jahre alt. 19 Patienten waren jünger als 40 Jahre.

Die brechenden Medien waren in allen Fällen klar.

An der Schprobentafel betrug die Sehschärfe 3/4 3/5 3/7. Die Nyktometerprüfung wurde mit Fernkorrektur durchgeführt. Die Refraktionen lagen im Bereich von + 2.5 bis - 2.0 D sphärisch. Jedoch in einem Fall von Makuladegene-

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Periphlebitis mit Makulaveränderungen	2
Chorioretinitis juxtapapillaris	1
Makuladegeneration	12
	insges. 46

- 17 *Mazzanti L und G Tola* Boll oculist 44 909 (1965) ref Zbl f d ges Ophthal 97 367 (1967)
- 18 *Pat- H* Verkehrsmedizin und ihre Grenzgebiete 16 Jahrg 1969 81
- 19 *Sack E* Verkehrsmedizin 15 191 (1968)
- 20 *Seferin S L Tour R L und Kershaw R H* Arch Ophthal (Chicago) 163 (1967)
- 21 *Schober H* Das Schen Fachbuchverlag Leipzig 1964
- 22 *Schmoger E* Medizintechnik I 13 (1964)
- 23 *Venturi G und U Volpi* Ann Ottal 86 65 (1960) ref Zbl f d ges Ophthal 80 331 (1960)
- 24 *Weinhold H* Medizintechnik I 11 (1964)
- 25 *Trendelenburg W* Der Gesichtssinn II Aufl Springer Verlag Berlin 1961
- 26 *VEB Carl Zeiss Jena* Registrier Nyktometer Druckschriften Nr 60 0760 1

Tabel 4
Adaptationsdauer bei 02 Visus am Nyktometer

Adaptationsdauer in sec	Anzahl der Augen
41- 60	1
61- 80	3
81-100	4
101-120	3

bis zu einer Adaptationsdauer von 60 Sekunden Nach Tabelle 4 haben dann alle 11 Augen (das 1 Auge der Spalte 41 60 sec gehört einer 22-jähriger Patientin) die die Sehscharfe 02 erreichen keine normale Adaptationsdauer

Von unseren 46 am Registrierer Nyktometer des VEB Carl Zeiss Jena geprüften Augen mit makularen Veränderungen und noch guter Sehscharfe beim Tagessehen zeigten 42 eine Störung der Sofortadaptation die sich in 23 Fällen in herabgesetzter Sehscharfe in 19 Fällen sogar in völligem Verlust der Sofortadaptation ausserte Bei 21 Augen von den insgesamt 23 mit herabgesetzter Sehscharfe liess sich daneben eine Verlängerung der Adaptationsdauer nachweisen

Blendempfindlichkeit

Die Sehscharfewerte bei Blendung sind in Tabelle 5 verzeichnet Bei der Beleuchtungsstufe 8 erreichten 34 Augen von insgesamt 46 keine normale Sehscharfe, hatten also eine erhöhte Blendempfindlichkeit Bei der Beleuchtungsstufe 64 waren 24 Augen noch erhöht blendempfindlich Dabei waren unter den Augen die bei Beleuchtungsstufe 8 erhöhte Blendempfindlichkeit zeigten die 19 Augen wieder anzutreffen bei denen die Sofortadaptation völlig aufgehoben war 12 von ihnen fanden sich auch wieder unter den erhöht Blendempfindlichen bei Beleuchtungsstufe 64

Sofortadaptation und Blendempfindlichkeit im Verlauf von Retinitis centralis serosa

4 Patienten mit Retinitis centralis serosa konnten wir während des Krankheitsverlaufes wiederholt am Registrierer Nyktometer des VEB Carl Zeiss Jena untersuchen einen davon allerdings erst nach 5 wöchiger Behandlung

Die Sofortadaptation ist während der Erkrankung in allen Fällen erheblich herabgesetzt Während die Sehscharfe beim Tagessehen mit Plusgläsern so korrigiert werden kann dass normale Werte erreicht werden ist das bei herab



Fig 3

Large hemangioma. Anterior wall presents a facet that molds the posterior wall of the eyeball.



Fig 4

Section of hemangioma. Hematoxylin Eosin - $\times 42$. Large endothelium lined blood containing spaces indicating a cavernous hemangioma.

Tabel 2
Sofortadaptation bei Makulaveränderungen.

Visus am Nyktometer	Anzahl der Augen	davon Visus an der Schprobentafel		
		5/4	5/5	5/7
0	19	9	5	5
0 1	12	0	3	3
0 2	11	6	2	3
0 3	4	2	2	—

normalen Streubereich wie er von uns gefunden wurde und auch von Lehnert und Schmidt angegeben wird. Es handelt sich dabei 2 \times um eine Chorioretinitis paracentralis, 1 \times um eine Chorioretinitis disseminata und 1 \times um eine Retinitis centralis serosa.

In Tabelle 3 und 4 sind die Zeiten angegeben, die für die erreichte Sehschärfe am Nyktometer benötigt wurden. Normale im Alter von 40–49 Jahren brauchen bei monokularer Prüfung für die Erlangung der Sehschärfe 0 1 im Durchschnitt 22 Sekunden, bei Berücksichtigung der Streuung bis 40 Sekunden. Auch die Altersgruppe 50 bis 59 Jahre, der einer unserer Patienten mit Visus 0 1 angehört, beansprucht normalerweise keine längere Zeit. Demzufolge erreichen nur 2 (der Patient ist 42 Jahre alt) von 12 Augen (s. Tab. 3) den Visus von 0 1 in einer normalen Zeit. Bei den übrigen 10 Fällen ist die Adaptationsdauer verlängert, d. h. der Anstieg der Sofortadaptationskurve ist flacher als normal. Die benötigte Zeit für die Sehschärfe 0 2 streut bei monokular geprüften 20–29-jähriger bis zu einer Adaptationsdauer von 40 Sekunden, bei den älteren Altersgruppen

Tabel 3
Adaptationsdauer bei 0 1 Visus am Nyktometer

Adaptationsdauer in sec	Anzahl der Augen
31–40	2
41–60	3
61–80	2
81–100	3
101–120	2



Fig 1

Left exophthalmos Left eye is pushed straight forward

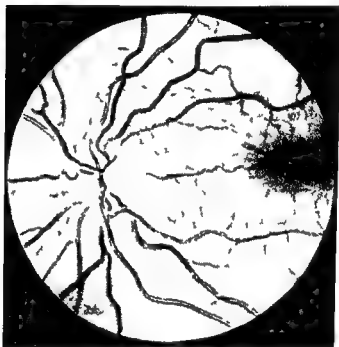


Fig 2

Posterior pole of the left eye showing retinal striae from disc to macular area

present Roentgen examinations of the skull and the orbits proved negative An angiography of the orbit demonstrated an abnormal displacement of the left ophthalmic vein

A Kronlein orbitomy was performed to explore the lateral and retrobulbar regions of the orbit When the index finger was introduced behind the eyeball an encapsulated tumor was easily separated from the surrounding tissues and removed The red firm tumor measured 30×21 mm and presented a facet in its anterior part which molded the posterior portion of the eyeball (fig 3) Histologically it consisted of endothelium lined blood containing spaces characteristic of a cavernous hemangioma (fig 4)

gesetzter Beleuchtung wie sie am Nyktometer herrscht nicht der Fall. Auch bei einem Patienten, der während des gesamten Verlaufes der Erkrankung auch ohne Korrektur über volle Sehschärfe bei Tagesschein verfügt und lediglich eine Störung des qualitativen Sehens (Metamorphopsie am Amsler Netz) aufweist, ist die Sofortadaptation erheblich herabgesetzt. In Tab. 8 sind die Untersuchungsbefunde eines Patienten zusammengestellt. Mit der ophthalmoskopisch nachzuweisenden Abheilung des Prozesses im Makulabereich erholte sich in unseren Fällen die Funktion der Sofortadaptation soweit, dass sie als normal zu bezeichnen ist. Bis zu dieser Erholung verging bei 2 Patienten ein Vierteljahr.

In Abb. 1 haben wir einige Kurven der Sofortadaptation wie auch die entsprechende Blendempfindlichkeit, die zu verschiedenen Zeiten der Erkrankung eines Patienten aufgenommen wurden und das Wiedergewinnen der Funktion während des Verlaufes der Retinitis centralis serosa erkennen lassen. dargestellt. Ein Übungseffekt wie er bei Normalen beobachtet wird (Lehnert und Schmidt Patz) konnte während der herabgesetzten Funktion der Sofortadaptation nicht nachgewiesen werden.

Bei allen 4 Patienten ist während der Erkrankung auch die Blendempfindlichkeit bei Beleuchtungsstufe 8 und 64 (Tab. 6, Abb. 1) erheblich in Mitleidenchaft gezogen. Aber auch sie kehrt mit Abheilung der Erkrankung in den Normbereich zurück.

Diskussion

Aus den Ergebnissen der vorliegenden Arbeit geht hervor, dass Sofortadaptation und Blendempfindlichkeit am Registrier-Nyktometer des VEB Carl Zeiss Jena bei makularen Erkrankungen dann schon stark verändert sind, wenn die Sehschärfe noch nicht beträchtlich herabgesetzt ist. Unsere Befunde bestätigen die Angaben der Literatur. So berichten Venturi und Volpi über starke Herabsetzung der Sehschärfe bei herabgesetzter Beleuchtung bei Patienten mit makularen Erkrankungen und über eine leicht verzögerte Dunkeladaptation, was vor allem im ersten Abschnitt der Kurve deutlich nachzuweisen war, geprüft am Goldmann-Weekers-Adaptometer. Auch Faraldi konnte bei differenzierter Prüfung des Lichtsinns am Goldmann-Weekers-Adaptometer bei Patienten mit erworbenen makularen Veränderungen Abweichungen von der Norm festzustellen. Mazzantini und Tola fanden bei 38 Patienten mit morphologischen Makulaveränderungen aber normalem Visus in 30 Fällen eine deutliche Herabsetzung des Visus mesopicus.

Die Blendempfindlichkeit, geprüft als Sehschärfe während Blendung am Registrier-Nyktometer, war bei einem beträchtlichen Teil unserer Patienten er-

The susceptibility of hemangiomas of the orbit to hormonal change the pregnancy in particular ■ emphasized

References

- 1 Walsh F B Clinical Neuro Ophthalmology Williams and Wilkins Baltimore p 955 1957
- 2 Watson W L & McCarthy W D Blood and Lymph vessel tumours. Cit by Reese A B Orbital tumours and their surgical treatment Amer J Ophthal 24 386 394 1941
- 3 Reese A B Tumours of the Eye Harper and Row New York p 411 1963
- 4 Reese A B Tumours of the Eye Harper and Row New York p 368 1963

Tabel 5
 Sehscharfe bei Blendung
 Die fettgedruckten Werte liegen innerhalb der Streubreiten Normaler 10-59 jähriger bei monokularer Prüfung

Beleuchtungsstufe	Anzahl der Augen mit Visus									
	00	01	02	03	04	05	06	07	08	09 10
1	48	2	1	-	-	-	-	-	-	-
8	11	7	10	7	3	2	-	-	-	-
64	-	1	6	10	7	4	8	7	2	1

The postoperative course was uneventful. The exophthalmos disappeared (fig 5) and two months after surgery the fundus presented normal features, the visual acuity improved to 6/6 and the visual field presented a normal configuration.

Discussion

The presence of an exophthalmos changing in size has been observed in orbital hemangiomas and usually linked to local bleeding. It is of interest however to note that vascular tumors can grow under the influence of endocrine factors and pregnancy in particular. Watson & McCarthy surveyed 1001 hemangiomas located at different sites of the body and pointed out that they occurred more often in females (65%) and are prone to start or increase rapidly in size with the onset of menses or at the beginning of pregnancy. In the eye, Reese observed in one patient the aggravation of a choroidal racemous hemangioma at the time of two pregnancies (3) and in another case the sudden growth of an orbital racemous hemangioma also during pregnancy (4).

In the patient reported in the present article, the onset of exophthalmos during puberty and its growth during pregnancy is additional evidence that such orbital tumors are susceptible to hormonal changes. The importance of these events in the differential diagnosis of orbital tumors is evident.

Summary

A 31 year old pregnant woman presented with a growing unilateral exophthalmos which had been first noted during puberty. Surgical exploration revealed an orbital cavernous hemangioma.



Fig 5
Post operative appearance

13	0.1 (0.7)	50	0.0 (0.2)	0.4 (0.8)	0.6 (1.0)	5/10 +1.5 = 5/4p	+	Makulareflex unregelmässig I rasipitate d Retina
14	0.1 (0.7)	63	0.0 (0.1)	0.4 (0.9)	0.8 (1.0)	5/5p +0.5 = 5/4p	+	Makulareflex unregelmässig Frazipitate d Retina
+104	0.2 (0.7)	108	0.0 (0.0)	0.2 (0.9)	0.55 (1.0)	5/4p Gl b n	+	Makulareflex unregelmässig I rasipitate d Retina
174	0.2 (0.7)	77	0.0 (0.2)	0.4 (0.8)	0.9 (1.0)	5/4p Gl b n	+	kein Ödem noch I rasipitate
+944	0.4 (0.7)	08	0.0 (0.2)	0.7 (0.9)	1.0 (1.0)	5/4	+	I pigmentverschie- bungen
+85	0.5 (0.7)	118	0.1 (0.2)	0.4 (0.9)	0.9 (1.0)	5/4	+	I pigmentverschie- bungen

Die Zahlen in Klammern sind die Sehschärfewerte des gesunden normallichtigen Auges. Die Sofortadaptationskurven und die Blendempfindlichkeit die an den mit + versehenen Tagen aufgenommen wurden sind in Abb. 1 dargestellt.

uns waren im April/Mai und Oktober/November die meisten und im Dezember die wenigsten Erkrankungen zu verzeichnen signifikant waren die Unterschiede allerdings nicht

Die Geschlechtsverteilung ergibt mit 42 Männern und 65 Frauen etwa das Verhältnis von 2:3 die Altersverteilung (Abb 1) umfasst Patienten von 15 bis 63 Jahren wobei die Erkrankungshäufigkeit gleichmässig ansteigt und nach einem Gipfel bei den 36 bis 40 Jährigen wieder kontinuierlich zurückgeht Eine Neuritis nervi optici ist sowohl bei Kindern als auch im höheren Alter selten Lediglich Kennedy & Carroll beschrieben mehrere Beobachtungen bei Kindern bei denen eine grössere Tendenz zum bilateralen Auftreten stärkere Begleitskopfschmerzen und überwiegend die Verlaufsform als Papillitis zu beobachten war In der Regel tritt die Sehnervenentzündung zunächst nur an einem Auge auf und – falls überhaupt – erst eine zeitlang später auch am anderen Immerhin hatten von unseren Patienten aber doch 12 eine Neuritis nervi optici zu gleicher Zeit an beiden Augen

Symptome

Unter den subjektiven Symptomen spielen die Angaben über Sehstörungen die grösste Rolle So wurden von 69 unserer Patienten als Initialsymptom Schleiersehen Verschwommensehen Schatten vor dem Auge oder Sehverschlechterung genannt wogegen bei den anderen 18 Kopfs- und Augenschmerzen als Druckschmerz oder ziehender Schmerz bei Blickbewegung im Vordergrund standen In diesen Fällen folgten Sehstörungen nach 1 bis 8 Tagen

Befunde

Obereinstimmend mit diesen subjektiven Angaben war unter den objektiven Befunden fast immer eine mehr oder minder starke Beeinträchtigung der Sehschärfe vorhanden Nur 4 Patienten hatten auf dem erkrankten Auge noch eine

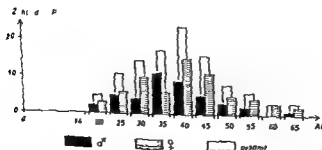


Abb 1
Altersverteilung von 107 Patienten mit Neuritis nervi optici

Tabel 6

Makulafunktion während Verlauf der Retinitis centralis serosa der Versuchsperson I(R A 33-jähr Mann seit 3 Tagen Flimmern v d re Auge

Dat d Untersuch	Visus wahrd Sofortadapt	benötigte Zeit 1 sec	Blendungsempfindlichkeit Visus bei Beleuchtungsstufe				Visus an Sehproben tafel	Störungen am Amsler Netz	ophthalmoskop Befund
			Visus bei Beleuchtungsstufe						
			1	8	64				
+30 1 69 + 82 122 152 192	00 (06) 01 (06) 00 (07) 00 (07) 00 (07)	- 48 - - -	00 (00) 00 (00) 00 (00) 00 (00) 00 (00)	00 (03) 02 (03) 00 (06) 01 (09) 00 (06)	01 (08) 06 (10) 06 (10) 06 (10) 03 (10)	5/10 5/15 5/15 5/15 5/15	+40 = 5/4 +20 = 5/4p +25 = 5/4p +25 = 5/4p +25 = 5/4p	+ + + + +	Makulaodem Makulaodem Makulaodem Makulaodem Makulareflex unregelmässig Präzipitate d Retina Makulareflex unregelmässig Präzipitate d Retina Makulareflex unregelmässig Präzipitate d Retina
252	00 (07)	-	00 (00)	01 (05)	06 (10)	5/15	+20 = 5/4p	+	
43	00 (07)	-	00 (00)	01 (09)	05 (10)	5/20	+20 = 5/4p	+	
143	015 (06)	47	00 (00)	01 (09)	05 (10)	5/35	+20 = 5/7	+	

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DIE NEURITIS NERVI OPTICI

VON

INGEBORG HEINRICH

Noch immer bringt das Krankheitsbild der Sehnervenzündung (Neuritis nervi optici) von Fall zu Fall erhebliche diagnostische und therapeutische Probleme mit sich egal ob der papillenferne Abschnitt als Neuritis *retrobulbaris* oder der papillennahe Optikusanteil als Neuritis *intraocularis* = Papillitis befallen ist. Wenn sich auch in vielen Fällen die Symptome spontan und schnell zurückbilden und oft sogar eine Restitution ad integrum erreicht wird, so ändern sich doch in anderen Fällen Funktionsverfall und pathologischer Papillenbefund oft lange Zeit nicht und es kommt trotz Anwendung zahlreicher therapeutischer Massnahmen zu folgeschweren Defektheilungen.

So steht der behandelnde Augenarzt eigentlich bei jeder Sehnervenzündung immer wieder vor einer Reihe unbekannter Faktoren von denen einige vielleicht zu klären sind wenn man ein grösseres Krankengut auswertet. Dies soll im Folgenden geschehen.

Eigenes Krankengut

Anamnese

Den Ausführungen liegen anamnestische Angaben und Befunde von 107 Patienten aus den letzten 6 Jahren zugrunde. In den einzelnen Jahren der Beobachtungszeit waren jeweils etwa gleich viele Patienten erkrankt.

Einige Autoren hatten eine *jahreszeitliche Häufung* der Erkrankung z. B. im Frühjahr (Miwa) oder in Vorfrühling und Herbst (Sugawara) gefunden. Bei

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und Nover sehen die Störung des Licht- und Farbensinns bei Retinitis serosa als so charakteristisch an, dass sie eine wertvolle Hilfe bei der Diagnostik in Fällen von geringgradigem objektiven Fundusbefund zu leisten vermögen.

Die Prüfung am Nyktometer während des Erkrankungsverlaufes stellt nach unseren Befunden eine ähnlich empfindliche Methodik zur Beurteilung der Makulafunktion dar wie die Prüfung des qualitativen Sehens am Amster Netzer.

Zusammenfassung

Patienten mit makularen Veränderungen aber guter Sehschärfe wurden am registrierbaren Nyktometer des VEB Carl Zeiss Jena untersucht. Dabei zeigte sich in 42 von 46 Fällen eine Störung der Sofortadaptation, die sich in herabgesetzter Sehschärfe und verlängerter Adaptationsdauer äusserte oder sogar in völligem Verlust der Sofortadaptation.

In 34 Fällen wurde eine erhöhte Blendempfindlichkeit nachgewiesen.

Daneben wird über Nyktometerbefunde während des Verlaufes von Retinitis serosa berichtet.

Auf den Wert der Nyktometer-Untersuchung als Funktionsprüfung in Fällen von Makulaerkrankungen mit noch guter Sehschärfe beim Tagessehen wird hingewiesen.

Literatur

- 1 Amster M. Ophthalmologica (Basel) 114: 248 (1948)
- 2 Aulhorn E. und H. Harms. Ber. Dtsch. Ophthalm. Ges. 66: 425 (1964)
- 3 Braun R. A. v. Graefes Arch. Ophthalm. 144: 41 (1941)
- 4 Broschmann D. Verkehrsmedizin und ihre Grenzgebiete 16. Jahrg. 1969: 73
- 5 Comberg W. Ber. Dtsch. Ophthalm. Ges. 59: 11 (1959)
- 6 Comberg W. Ber. Dtsch. Ophthalm. Ges. 53: 6 u. 329 (1940)
- 7 Comberg W. Untersuchungsmethoden. Lichtsinn. in: Der Augenarzt Bd. 2 v. A. Velhagen. VEB Georg Thieme Leipzig 1959
- 8 Consul M. V. und Charan H. Amer. J. Ophthalm. 58: 1007 (1964)
- 9 Faaldi I. Rass. vital. Ocul. 53: 1-3 (1964) ref. Zbl. f. d. ges. Ophthalm. 99: 53 (1968)
- 10 Forsius H., Krause U. und A. W. Eriksson. Acta Ophthalm. (Kbh.) 42: 25 (1964)
- 11 Forsius H., Krause U. und A. W. Eriksson. Acta Ophthalm. (Kbh.) 40: 55 (1964)
- 12 Heinisius E. Klin. Mbl. Augenheilk. 106: 443 (1941)
- 13 Hekind P. und S. J. J. M. Amer. J. Ophthalm. 64: 314 (1967)
- 14 Jaeger W. und Nover A. v. Graefes Arch. Ophthalm. 152: 111 (1951)
- 15 Lehnert W. und J. Schmidt. Z. Altersforschung 10: 27 (1967)
- 16 Lehnert W. und R. Schmidt. Verkehrsmedizin 13: 314 (1966)

krankung unabhängig fanden sich darüber hinaus einige Male degenerative Veränderungen im Maculabereich sowie arteriosklerotische diabetische oder hypertensive Gefäßveränderungen

Bei unseren 107 Neuritis Patienten trat 9mal die Erkrankung zunächst nur einseitig auf 45mal war das rechte und 50mal das linke Auge betroffen 14 dieser Patienten bekamen später d. h. nach 4 Wochen bis mehreren Jahren eine Neuritis auch am anderen Auge Weitere 12 Patienten hatten – wie oben schon erwähnt – an beiden Augen zu gleicher Zeit eine Sehnervenerntzündung Zweimal traten Rezidivkrankungen am selben Auge auf einmal nach 3 Wochen einmal nach 3 Jahren

Ätiologie

Die eingangs erwähnten diagnostischen Probleme bei der Neuritis nervi optici betreffen vor allem die Klärung der Krankheitsursache Man fahndet nach durchgemachten Viruserkrankungen (Crippe!) bakteriellen Infektionen internen Krankheiten endokrinen Störungen und diskutiert vor allem die Beziehung „en zur Encephalomyelitis disseminata (Hyllsted & Møller) Wir führten aus diesem Grunde bei unseren 107 Patienten insgesamt 320 konsiliarische Untersuchungen in anderen Fachkliniken durch (Abb 3) Wie oft sich dabei pathologische Befunde erbogen geht ebenfalls aus der Abb 3 hervor Es wurde bei etwa jedem zweiten untersuchten Patienten im *HNO Bereich* ein pathologischer Befund meist eine Tonsillitis gefunden 12mal wurde daraufhin noch während der augenklinischen Behandlung eine Tonsillektomie durchgeführt Ähnlich häufig fanden sich Befunde bei Untersuchungen in der *Zahnklinik*

Da in der ophthalmologischen Literatur angegeben wird dass die Multiple Sklerose in 10 5% (Tizemski & Kusowicz) bis 16 4% (Lynn) als Ursache der Sehnervenerntzündung infrage kommt wurden an diesbezügliche *neurologische Untersuchungen* besondere Erwartungen geknüpft Sie ergaben aber nur 21mal – also nur bei jedem Vierten der neurologisch untersucht wurde – etwas Auffälliges Allerdings sind die aetiologischen Zusammenhänge zu Anfang oft schwer zu klären weil die Sehnervenerntzündung den neurologischen Symptomen unter Umständen Jahre vorausgehen kann Im neurologischen Schrifttum wird die Multiple Sklerose in 39 3% als Ursache der Neuritis (Scheid Bradley) genannt Brain hält nur die einseitige Neuritis für eine Folge der Encephalomyelitis disseminata Bei unseren Patienten war eine solche 5mal zum Zeitpunkt der Augenerkrankung zu sichern und 8mal wahrscheinlich zu machen In den anderen Fällen fanden sich Nikotin bzw Alkoholabusus (6 \times) Poliomyelitis (1 \times) und Lues cerebrospinalis (1 \times)

Die *internistische Untersuchung* ergab 15mal pathologische Befunde doch kamen die meisten davon – abgesehen vom Diabetes – nicht als Ursache der Neuritis nervi optici infrage Bei 16 Patienten liess sich nirgendwo etwas Pa

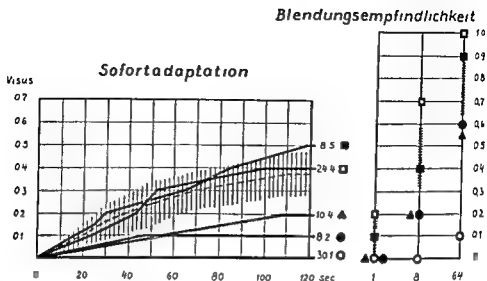


Abb 1

Sofortadaptation und Blendungsempfindlichkeit der Versuchsperson I während des Verlaufs der Retinitis centralis serosa des rechten Auges. Zum Vergleich ist die Mittelwertskurve der Sofortadaptation (gestrichelte Linie) mit der Standardabweichung s (senkrechte Striche) die durch einmalige Untersuchung des rechten Auges von 20 normal-sichtigen

30-39-jährigen Versuchspersonen gewonnen wurde mit eingezeichnet. Mittelwert und Streuung der Blendungsempfindlichkeit der gleichen Normalgruppe sind punktiert gezeichnet.

Blendungsempfindlichkeit am 30.1.69 ○
8.2.69 ●
10.4.69 ▲
24.4.69 □
8.5.69 ■

höht. Im Schrifttum wird meist über die Readaptationszeit, das ist die Erholungszeit für die Schärfe nach starker Blendung, berichtet. Diese ist bei makularen Erkrankungen nach Forsius, Ericsson und Krause, Henkind und Siegel, Consul und Charan erheblich verändert und sie gilt nach Seferin, Tour und Kershaw als schärferes Kriterium als die Schärfe.

Nach unseren Ergebnissen erweist sich die Untersuchung am Registrier-Nyktometer des VEB Carl Zeiss bei makularen Veränderungen als eine sehr empfindliche Funktionsprüfung. Die Klagen der Patienten können besser objektiviert werden. Damit findet das Gerät neben der Untersuchung zur Verkehrstauglichkeit (Broschmann) hier einen weiteren Einsatzbereich. An unseren 4 wiederholt untersuchten Fällen von Retinitis centralis serosa konnten wir feststellen, dass sich die während der Erkrankung sehr stark herabgesetzte Sofortadaptation wieder erholt. Das konnten auch Jaeger und Nover bei Retinitis centralis serosa in 4 Fällen am Nyktometer nach Comberg nachweisen. Jaeger

normale Sehscharfe 52mal betrug sie weniger als 1/10 4 Augen waren bereits erblindet (Abb 2)

Keiner der Patienten hatte noch ein normales *Gesichtsfeld* Bei jedem zweiten Patienten waren zentrale paracentrale oder Ringskotome vorhanden bei den anderen bestanden Einengungen der Aussengrenzen und Ausfälle in der Gesichtsfeldmitte

Am *Augenhintergrund* hatten 43 Patienten bei Krankheitsbeginn einen normalen Papillenbefund als Ausdruck einer *retrobulbaren* Lokalisation der Neuritis Die Diagnose »Schnervenentzündung« stützte sich in diesen Fällen auf die nachweisbaren Funktionsstörungen In den übrigen 76 Fällen war die Papille hyperaemisch oedematös unscharf begrenzt 2 T fanden sich Blutungen und Gefäßeinscheidungen 18mal bestand eine Optikusatrophie Von der jetzigen Er

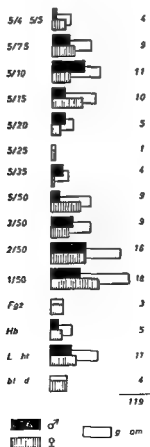


Abb 2
Visuswerte der erkrankten Augen bei Klinikaufnahme

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ORBITAL HEMANGIOMA GROWTH DURING PREGNANCY

BY

HANAN ZAUBERMAN and MOSHE FEINSOD

Recurrent exophthalmos has been observed in orbital hemangiomata and explained on the basis of recurrent hemorrhages

The following report will deal with a case of recurrent exophthalmos beginning with puberty and exacerbated by pregnancy

Case Report

A 31 year old woman has suffered from a mild left proptosis since 1951. The condition remained stable until 1963 and repeated exophthalmometries showed readings of 18 mm in the right eye and of 20 mm in the left eye and visual acuities of 6/6 in each eye. In December 1963 when the patient was in the fourth month of her pregnancy the left exophthalmos began growing and the patient attended the eye clinic with a complaint of increasing proptosis in the left eye and a mild blurring of vision.

The examination showed a visual acuity of 6/6 in the right eye and of 6/9 in the left eye. The intraocular pressure was within normal limits. Hertel's exophthalmometer showed readings of 19 mm in the right eye and of 23 mm in the left eye. The left eye was displaced straight forward (fig. 1). There was a mild limitation of abduction of the left eye but the patient did not complain of diplopia.

The left fundus showed changes in the posterior pole consisting of edema and retinal striae from the disc to the macular area (fig. 2). This area was 3 diopters higher than the surrounding parts of the fundus. The right fundus was normal. The left visual field presented an upper nasal quadrant defect. No neurological abnormalities were

weist auf die Schwierigkeiten bei der einzuschlagenden Therapie und bei der Beurteilung der Prognose hin

Therapie

Aus diesen Gründen kann auch die Therapie der Neuritis nervi optici nur selten eine kausale sein. Sie besteht in allgemeiner (Bettruhe) und örtlicher Ruhigstellung (Mydriasis Verband) und aus allgemein wie örtlich entzündenden entzündungshemmenden robrierenden und durchblutungsfördernden Massnahmen. Verwendet werden Irgapryn Tomanol Tanderil als Injektionen Tabletten oder Suppositorien Cosaldon Complamin Niconacid als Tabletten Injektionen oder Infusionen Kalium jodatum Vitamin B Präparate Wärme und un-

spezifische Reiztherapie (Schulz & Kment) (Abb. 4)

Darüberhinaus wurden – vor allem bei akuten Verlaufsformen – frühzeitig Cortisonpräparate (oral oder parenteral) gegeben in der Vorstellung rasch Entzündung und Exsudation zu unterdrücken und somit toxische Gewebsauswirkung

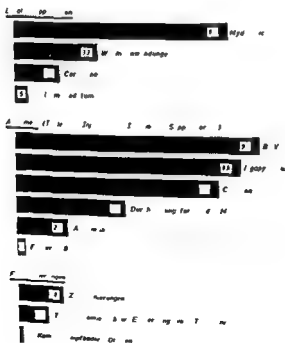


Abb. 4
Behandlung bei Patienten mit Neuritis nervi optici

- 12 *Aichmaier H* Ein verbessertes Instrument zur retrograden Sondierung und Wiederherstellung verletzter Tränenrohren Klin Mbl Augenheilk 1967 150 393-400
- 13 *Neubauer H* Grundsätze der Lidchirurgie Klin Mbl Augenheilk 1965 147 313-335

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To reconstruct slit canaliculi of any origin we start in the usual manner we make intermarginal incision on each lip between the skin and canalicular epithelium. Then we unite the wound not by one and two sutures – as recommended in most textbooks – but by several U stitches and single sutures too (Fig 7). Otherwise the canaliculus may reopen (13) or get gaps which would hinder the normal outflow of tears.

Summary

It was recommended: a) different methods to find the torn end of the lacerated canaliculus; b) the retrograd cannula to reconstruct the lacerated canaliculus to determine the site of the obstructed part of the canaliculus; to make retrograde an artificial lacrimal punctum; c) Hyasone own blood serum and cysteine to apply at probing for obstructed canaliculus; d) a correct method to close the slit canaliculus.

References

- 1 Korchmaros I. Eingriff beim Diverticulum des Tränensackes. Ber. österr. ophthal. Ges. Bruder Hollinek 1962, Wien, pp. 16–180.
- 2 Morrison F. An aid to repair of lacerated tear ducts. Arch. Ophthal. 1964, 72: 341–342.
- 3 Korchmaros I. Mechanical treatment for canaliculitis (Under publication).
- 4 Korchmaros I., Salminen L. Retrograd cannula for lacrimal canaliculi. Acta Ophthal. 1967, 45: 209–210.
- 5 Graeves D. F. Operation for the repair by primary suture of a recently divided lower canaliculus. Cit. by Stallard H. B. Eye surgery. Wright J. 1950, Bristol, p. 255.
- 6 Kellner W. Die Versorgung von Verletzungen der Tränenröhrchen mit Hilfe der Retrogradsonde. Klin. Mbl. Augenheilk. 1960, 131: 93–96.
- 7 Alekseev B. N. Application of a special sound during restorative surgery on the lacrimal canaliculus. Vestn. Oftal. 1961, 74: 80–85.
- 8 Worst J. G. F. Method for reconstructing torn lacrimal canaliculus. Amer. J. Ophthal. 1962, 53: 520–522.
- 9 Medgyasay A., Szabo Gy. Instrument for reconstruction of canaliculi. Szemészet (Budapest) 1966, 103: 115–116.
- 10 Rodenhauer J. H. Zur chirurgischen Versorgung verletzter Tränenröhrchen. Klin. Mbl. Augenheilk. 1966, 148: 892–895.
- 11 Horodenska A. Surgical procedure in injuries of lacrimal canaliculi. Klinika Oczna 1966, 36: 593–596.

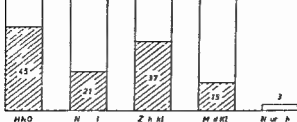


Abb 3

und Ergebnis 320 konsiliarischer Untersuchungen bei 107 Patienten mit Neuritis nervi optici

gisches finden 24 Patienten hatten dagegen mehr als einen krankhaften Befund 4 sogar 3

versucht man nun aus den vielen Einzelbefunden Rückschlüsse auf die Ätiologie der Augenerkrankung zu ziehen so kommen von den vielen Befunden in erster Linie die Multiple Sklerose (13 X) der Diabetes (6 X) in Alkoholabusus (6 X) die Lues cerebrospinalis (1 X) infrage dazu kommen in anderen Fällen unmittelbar vorausgegangene Erkrankungen wie Zoster ophthalmicus Zahnextraktionen etc

Interessant war bei 31 Patienten also knapp 1/4 unseres Krankengutes die Ursache der Sehnervenentzündung zu finden in 3/4 der Fälle aber in einer Vielzahl pathologischer Befunde in anderen Fachgebieten ungeklärt zumindest fraglich geblieben Dies liegt vor allem an der vorsichtigen Interpretation der in der HNO und Zahnklinik erhobenen Befunde

Schon an anderen Orten wurde beobachtet dass im Gegensatz zu früher Nebennierenfunktionen viel seltener als Ursache einer Neuritis infrage kommen (et Calmettes Coll) Boros Wu Rucker Carroll Trzcinska Dabrowski vize geben in ihrem Krankengut 1/3 der Fälle als ätiologisch ungeklärt Cibis Otradovec & Votockova blieben es 50% bei Novak 68 4% sogar 75% also ähnlich wie jetzt bei uns

Die Zahlen hängen natürlich von Herkunft und Zusammensetzung des eigenen Krankengutes von der gerade vorherrschenden Lehrmeinung und von der mehr oder minder subjektiven Deutung konsiliarisch erhobener Befunde Auch bringt erst die Beobachtung des weiteren Krankheitsverlaufs Klarheit und dann wenn weitere Symptome im Laufe der Zeit hinzugekommen

merhin beleuchtet alles dies die eingangs aufgezeigte Problematik

The camera units of both instruments are fitted with a spherical and planar mirror and AGA Thermovision® with an optical system of lenses (germanium). The object is scanned horizontally (rotating element) and vertically (oscillating mirror). The incoming infrared radiation is focused on the detector which is a InSb crystal.

The display unit is a modified oscilloscope. (The signal from the detector is preamplified and processed before being used to modulate the intensity of the beam in the picture tube. The beam sweeps across the tube face in a pattern corresponding to the scanning pattern of the camera and this permits simultaneous viewing and recording. A picture of horizontal lines is formed on the screen, each line consisting of a certain number of dots. The light intensity of each dot is proportional to the infrared radiation emitted by the specific point investigated on the surface of the object.) On the black and white picture thus produced, called grey tone picture, the hot areas are portrayed in light shades of grey and the cool areas in darker tones.

If isotherms are used, these show up as white areas and this enables areas of identical temperatures to be easily distinguished. Isotherms can be superimposed along the entire grey tone scale.

Recording

The thermal picture displayed on the screen of the oscilloscope is photographed either with a polaroid black and white or a 35 mm colour film. If filters of different colours are placed between the viewing screen and the colour film, one for each isotherm and each colour is exposed on the same frame, a thermal picture is produced on which temperature differences can be easily evaluated.

In Table 1 the technical features of the two thermographs used are compared. A picture temperature range of 5° C and an isotherm width of 0.25° C (AGA Thermovision®) and 0.125° C (Bofors Infrared Camera) were used as standards. In order to obtain maximum magnification the thermal picture was electronically expanded and thereby also the isotherm width. Consequently one scale unit is the distance between the first and the third mark on the scale, was not equal to 1° C. (For conversion into Centigrades the factor 0.75 should be used.)

In the AGA Thermovision® the entire eye is portrayed if maximum magnification is used. For this reason each eye was examined separately. The temperature levels of the eyes were kept constant by comparing the energy emitted by each eye with the energy emitted by an ambient controlled temperature reference.

Absolute standardization of the experimental conditions was not possible but

dert und 16mal trat eine temporäre Abblutung auf. Obwohl in diesen Fällen also eine Verschlechterung des Papillenbefundes eintrat, verbesserte bzw. normalisierte sich auch in der Mehrzahl dieser Fälle der Visus. Dieser scheinbare Widerspruch zwischen objektivem Papillenbefund und Funktion ist auch bei anderen Optikusprozessen zu beobachten, worauf u. a. Nover am Beispiel von Patienten mit Hypophysentumoren hingewiesen hat.

Prognose

Wie die Auswertung dieser Krankengeschichten zeigt, kann eine Sehnervenerkrankung abheilen, ohne dass nachweisbare Schädigungen am Sehnerven zurückbleiben. Tritt im Laufe der Zeit eine Papillenabblutung auf, so muss dies nicht unbedingt auch mit einer Verschlechterung der Funktion einhergehen. In einigen dieser Fälle beobachteten wir eine Funktionsverbesserung, ja sogar eine Normalisierung. Prognose und Wiederherstellungsvermögen hängen von der Krankheitsursache und -dauer ab. Darüber hinaus spielt offenbar eine Gefäßkomponente und das Lebensalter eine Rolle, denn bei jüngeren Patienten sind – wie es auch Earl & Martin fanden – die Endresultate besser als bei älteren.

Zusammenfassung

107 Patienten (42 Männer, 65 Frauen), die in den letzten 6 Jahren wegen einer Neuritis nervi optici stationär behandelt wurden, standen in einem Alter von 13 bis 63 Jahren. Der Erkrankungsgipfel lag bei den Männern zwischen 31 und 35 Jahren und bei den Frauen zwischen 36 und 40 Jahren. 12mal waren zu gleicher Zeit beide Augen befallen, 14mal erkrankte das zweite Auge einige Zeit später. Fast immer waren Sehstörungen das Initialsymptom und dementsprechend Visusminderung und Gesichtsfeldausfälle vorhanden. 76mal bestand ein pathologischer Papillenbefund.

Die Ätiologie liess sich nur in einem Drittel der Fälle klären, was an der Schwierigkeit liegt, die konsiliarisch in anderen Fächern erhobenen Befunde zu interpretieren. Eine Multiple Sklerose konnte 5mal gesichert und 8mal wahrscheinlich gemacht werden.

Die Therapie wird beschrieben; sie führte in einem hohen Prozentsatz zu einer Verbesserung der Funktion, auch dann, wenn ein pathologischer Papillenbefund verblieb. Die durchschnittliche Behandlungsdauer betrug 21,5 Tage.

Anh. 1: Brief des Verfassers

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eye the difference being statistically significant ($P < 0.01$). In 12 of the 18 cases the affected eye was warmer by 0.5 scale units or more than the healthy fellow eye. As the optical and thermal resolutions are relatively small in the two thermographs used an elevated temperature of the affected eye was considered as abnormal only if the temperature difference between the two eyes was 0.5 or more scale units. As the iridocyclitis subsided the temperature of the eye gradually decreased. In view of the fact that hyperaemia of the pericorneal vessels and uveal tissue is associated with iridocyclitis this is not surprising.

Fig. 1 shows a histogram of the temperature difference between the affected eye and the healthy fellow eye. The mean value of the difference is statistically significant ($P < 0.01$).

In 3 of the 6 cases in which a derivative of adrenalin was instilled in both eyes the temperature of the affected eye increased as compared with that of the healthy eye. This drug causes constriction of the conjunctival and pericorneal vessels of the healthy eye and this results in blanching of the latter. The pericorneal vessels lying at a deeper level are not affected in acute iridocyclitis. The difference between the cases in which 10 per cent Neosynephrine® was instilled and those in which the drug was not applied was not statistically significant.

Out of the 5 cases of anterior uveitis associated with posterior uveitis the affected eye was warmer by 0.5 scale units than the healthy fellow eye in 3 cases. In 2 of these latter cases a mild anterior inflammation co-existed which might have been involved in the elevated temperature. In 1 of the 2 cases of choroiditis the affected eye was warmer than the healthy fellow eye.

In the two cases of retrobulbar tumour the affected eye was warmer than the healthy fellow eye. One of these patients had exophthalmos and the histological examination showed the retrobulbar tumour to be meningioma. In the other case a pathological report was not available.

Out of the 5 cases of choroidal tumour the affected eye was warmer than the healthy fellow eye in 3 cases. In one of these latter cases the histological examination showed the tumour to be a malignant melanoma and in the other two cases a pathological report was not available. Out of the remaining two cases of the former group one patient had only one eye, the fellow eye having previously been enucleated. In the other case in which there was a metastatic mammary carcinoma to the choroid the healthy eye was warmer than the affected eye.

In 3 cases of tumour of the iris, cornea and choroidea respectively the tumour could not be portrayed thermographically. This was rather surprising particularly with regard to the choroidal tumour as the latter was relatively large, infiltrated the ciliary body and appeared to be malignant. The probable reason was that the magnification was insufficient and the optical and thermal resolutions were too small in the thermograph.

gen und das Oedem des Opticus zu beseitigen und den Druck von den Sehnervfasern zu nehmen

Die Applikation erfolgte als Stosstherapie mit einer Anfangsdosis von 60 bis 80 mg in der Regel kam es auf eine Gesamtmenge von 450 bis 500 mg in einzelnen Fällen in denen eine MS gesichert war aber auf erheblich mehr weil eine Langzeitbehandlung notwendig war Im übrigen variierten wir die Dosis je nach dem Grad der Visusminderung

Zahlreich sind in der Literatur die Arbeiten die sich mit der Wirksamkeit (Neubauer & Karges, Doden Yokoyama, Kaneko Nakai & Taniguti) bzw Unwirksamkeit (Kazdan & Kennedy, Rucker Giles & Isaacson Oksala Angstwurm & Frick Glatzel & Lungershausen) der Nebennierenrindenhormone bei Neuritis nervi optici befassen Ein abschliessendes Urteil ist insofern schwer möglich als fast immer auch gleichzeitig andere Medikamente gegeben werden und gar nicht selten auch Spontanheilungen vorkommen Entscheidend ist der frühzeitige Behandlungsbeginn in den ersten 10 Tagen doch lässt sich auch dann die Erkrankungsdauer nicht signifikant kurzen (Graeber)

Behandlungsdauer

Die Dauer des Klinikaufenthaltes betrug bei unseren 107 Patienten durchschnittlich 21,5 Tage (bei Graeber 26,28 Tage bei Nover 22 Tage) im kürzesten Fall 6 im längsten 92 Tage weil es zu Rezidiven gekommen war

Verlauf

Der Verlauf einer Neuritis nervi optici lässt sich am besten aus dem Vergleich der Befunde bei Krankheitsbeginn und -ende beurteilen Soweit es die *Sehscharfe* betrifft (vergl. Abb. 2) hatten und behielten 4 Patienten eine normale Sehscharfe Bei den übrigen 115 Augen bestand eine mehr oder minder ausgeprägte Visusminderung die in 2 Fällen noch zunahm 5mal unverändert blieb und sich in 90 % besserte Insgesamt 57,14 % verliessen die Klinik mit normaler Sehscharfe

Ähnlich verhielt es sich mit den *Gesichtsfeldausfällen* die in keinem Fall grosser wurden 106 der 119 Neuritisfälle hatten bei Klinikentlassung wieder normale Aussengrenzen 1/3 hatte keine zentralen Ausfälle mehr in 60 Fällen waren sie kleiner geworden

Von den 43 unserer Neuritisfälle die bei Klinikaufnahme einen regelrechten *Papillenbefund* hatten bekamen 10 trotz aller Behandlung doch noch eine temporale bzw. totale Atrophie die anderen 33 blieben unauffällig Die bei 18 schon zu Beginn vorhandene Papillenabblässung (16mal temporal 2mal total) änderte sich während des Klinikaufenthaltes nicht Der Papillenbefund der übrigen 58 normalisierte sich 15mal besserte sich 20mal blieb 7mal unverändert

In 2 of the 5 cases of choroidal neoplasm histological examination showed the tumour to be malignant In 1 case malignancy was suspected because the patient had a history of enucleation of the fellow eye on account of malignant choroidal tumour which had been confirmed histologically In the other 2 cases a pathological report was not available

All these patients were examined by thermography In 37 patients only one eye and in the other both eyes were affected Eleven of these 38 patients were examined by thermography on several occasions

Twenty patients were examined in a sitting posture 10 of these without a mirror and the other 10 patients prone with a mirror suspended in front of them and angled at 45° From this mirror the radiation coming from the eye is reflected into the camera The other 18 patients were examined prone under anaesthesia after the application of a blepharostat and the instillation of an indifferent volatile solution This was done to avoid desiccation of the cornea These latter patients were examined with a mirror which was suspended in front of them and angled at 45° Twenty patients kept their eyelids apart spontaneously

In 5 of these 18 patients the anaesthetic was tetracaine combined with the instillation of physiological NaCl in 2 and Isopto Plain in 3 patients In the other 13 cases anaesthesia was produced with Novosin and was combined with the instillation of Methocel at intervals from 5 to 10 minutes In 4 cases the examination was carried out both with and without a blepharostat In 6 cases the patient was examined after the instillation of an adrenalin derivative

Forty one patients with healthy eyes were identically examined and were used as controls Twelve of them were examined in a sitting posture without a mirror On the other 29 patients the examination was carried out with the patient prone and a mirror placed in front of them In 4 of these latter cases a blepharostat was used

Results

Table 2 shows the temperature difference between the affected and healthy eye in the 38 cases in this series the difference being expressed in scale units

In the 18 cases of unilateral acute iridocyclitis the following observations were made In 14 of them the affected eye was warmer than the healthy fellow

* Isopto Plain® (5 mg/ml) Alcon Universal Ltd Fort Worth Texas U S A

* Novosin® (0.4%) Dr A Wander AG Bern Schweiz

* Methocel® (2%) Dr E Breschlin AC Winterthur Schweiz

*Universitätsaugenklinik Aarhus
(Chef Professor Viggo A Jensen)*

MIT DER HAND BEDIENTES SCHALTPULT ZUM MOTORISIERTEN OPERATIONSMIKROSKOP MODELL II DER FIRMA CARL ZEISS OBERKOCHEN

VON

VIGGO A. JENSEN

Das Schaltpult welches normalerweise zum motorisierten Operationsmikroskop Modell II der Firma Carl Zeiss gehört muss unter dem Behandlungstisch an gebracht und vom Chirurgen am besten in sitzender Stellung mit den Füssen bedient werden. Nach meinen Erfahrungen ist das Schaltpult etwas umständlich und unbequem und mit den Schuhen wie man sie in Operationszimmern benutzt schwierig zu bedienen. Ausserdem kann der harte Aufhang des Mikroskopes nicht vollständig ausgenutzt werden da der Chirurg an seine Stellung am Behandlungstisch gebunden ist und sich nicht fort bewegen kann ohne die Fühlung mit dem Schaltpult zu verlieren.

In Zusammenarbeit mit dem dänischen Vertreter der Firma Zeiss die Firma Brock & Michelsen in Kopenhagen* ist es gelungen ein kleineres Schaltpult zu konstruieren das mit Hilfe von Tasten auf die man mit den Fingern drückt, bedient wird wodurch es möglich ist selbst ganz kleine Korrekturen von sowohl Höheneinstellung dem kontinuierlichen Ändern der Vergrößerung der Fokussierung und der automatischen Mitteneinstellung von letzterer vorzunehmen. Wie aus der Abbildung hervorgeht ist an der linken Seite des Mikroskopaufhanges mit Hilfe einer gewinkelten Platte und 3 Bolzen eine vierseitige Metallkassette (12 x 18 x 5,5 cm) angebracht. Von den 7 Jantz Drucktasten wirkt jede auf ihren Burgess Mikroumschalter. Sie sind mit anderen Federn ausge-

* Brock & Michelsen Vesteregade 32 1456 Kopenhagen K.
Eingegangen am 7. Februar 1970

Disease	No of Cases	Patients Record No	Date of Examination	Affected Eye	Healthy Eye
			25 7/3 49 1/2	+ 17(2) + 01(1)	+ 18 + 04 + 02 + 15
Anterior Associated with Posterior Uveitis	5	S V 981003 H C 480710 G A 150913 S L 420302	5/3 12/3 12/4 20/3	+ 03 + 07 + 05	 + 06 + 04
Choroiditis	2	E S 450410 W L 090714 I P 491017	20/3 29/4 21/2	+ 06 + 01	+ 04 + 03
			3/3 73 10/1	 + 01	+ 01 + 04
Choroidal Tumour	5	K E 400103 T B 221029 J M 260711 G S 310222 P B 021013 B A 021223	29/4 9/1 28/2 29/4 23/4 40	+ 05 + 04 + 02 + 03	 + 04 Iritis
Retrobulbar Tumour	9	O E 110828 U M 110420	193 16/4	+ 10 + 05	
Conjuction of the Eyeball + Iridodialysis	1	H M 540120	29/1		+ 10
Episcleritis	1	L C 510707	24/2		+ 01
Ian phthalmitis	1	W F 060750	24/1	+ 07	
Bilateral	1	L I 06017	2/2	+ 12	
Central Retinitis			7/2		+ 04
Left eye more affected than right eye					
Tumour of the iris	1	C M 403115	7/3		+ 02
Tumour of the Cornea	1	K L 060124	14/4		+ 04
(Histologically confirmed malignant Melanoma)					

Literatur

- Angstwurm H & E Frick* Munch med Wschr S 1718 1964
Boros B & W G Bradley Dis nerv Syst 29 668 1968
Braun W R Trans ophth Soc U Kingd 54 221 1934
Carroll F D Am J Ophthal 35 75 1952
Carroll F D J Calvet L Calmettes & J Coll Rev Oto neuro ophtal 39 43 1967
Cibus P Klin Mbl Augenhk 102 205 1939
Doden W 7 Tg Osterr Ophthalm Ges 1 3662 ref Zbl ges Ophth 57 193 1963
Earl C J & B Martin Lancet 93 200 1967
Giles C L & D Isaacson 110 Ann Meet Sect on Ophth Amer Med Ass New York 28 VI (1961) ref Zbl ges Ophthalm 35 210 1962
Glatzel J & E Lungershausen Med klin. 64 1157 1969
Graeber W Klin Mbl Augenhk 148 811 1966
Hyllested A & P M Moller Acta ophthal (kbh) 39 655 1961
Kadan P & R J Kennedy Arch of Ophthalm 53 100 1955
Kennedy C & F D Carroll AMA Arch Ophth 63 747 1960
Lynn B H Trans ophth Soc U Kingd 79 701 1960
Miwa S Chuo Ganka Iho 30 7 1938 ref Zbl ges Ophthalm 42 382 1939
Neubauer H & E Karges Klin Mbl Augenhk 134 615 1959
Nover A Fortschr Med 85 993 1967
Nover A Neurol Psychiatr 30 230 1962
Oksala A Ophthalmologica 148 13 1964
Otradovc I & I Votockava Ccl Oftal 16 210 1960 ref Zbl ges Ophth 31 271 1960/61
Rucker C Trans Amer Acad Ophthalm a Otolaryngol 60 93 1956
Schult J & H Kment Klin Mbl Augenhk 146 833 1965
Sugawara S Sh Acta Soc Ophthalm Jap 62 304 1958 ref Zbl ges Ophthalm 44 309 1958
Trcinska Dabrowska Z & H Kosowic Klin Oczna 34 383 1964 ref Zbl ges Ophthalm 94 155 1965
Wu T Über die Ursachen und das zeitliche Auftreten der Neuritis retrobulbans Med Diss Hamburg 1938
Yokoyama H & Kaneko Y Nakai & Taniguchi J clin ophth 13 259 1964 ref Zbl ges Ophth 93 237 1965

Table 2

Temperature Difference⁽¹⁾ between Affected Eye and Healthy Fellow Eye in the 38 Cases in This Series

Disease	No of Cases	Patients Record No	Date of Examination	Affected Eye	Healthy Eye		
Acute Irido cyclitis	18	D A 370312	1968 18/12	+ 1.2			
			H A 170416	18/12	+ 2.0		
				1969 24/1	± 0		
		28/1		+ 0.2			
		L E 090321	2/3		+ 1.0		
			3/3		+ 0.2		
			6/3		+ 0.9		
		L B 290330	27/2	+ 1.0			
			3/3	± 0.4			
			5/3	+ 0.5			
		Recurrence			6/3	± 0	
					12/3	+ 2.5	
					24/4	+ 0.5	
				28/4	+ 0.5 + 1.0 ⁽²⁾		
				K I 060301	7/3	+ 0.1	
13/3				+ 0.9			
S H 270225	27/2			+ 1.0			
6/3				+ 0.4			
13/3				+ 0.4			
S M 571125	5/3			+ 1.0			
7/3	+ 0.3						
12/3	± 0						
A S 441205	4/2	+ 0.3					
E T 300919	7/2	+ 0.5					
N S 150504	25/3	+ 0.7					
W E 441025	16/4	+ 3.5 + 2.8 ⁽⁴⁾					
S B 290604	22/4	+ 1.0 + 0.5 ⁽¹⁾					
28/4	+ 1.3 + 0.8 ⁽¹⁾						
O B 441027	17/4	+ 1.0 + 2.5 ⁽³⁾					
22/4	+ 0.5 + 0.5 ⁽¹⁾						
M M 450112	30/4	+ 2.0 ± 0 ⁽¹⁾					
2/5	+ 0.5 + 0.5 ⁽¹⁾						
7.5	+ 0.7 + 0.5 ⁽²⁾						
L V 460712	16/4	+ 0.3					
A H 051019	28/4		+ 0.3 + 0.3 ⁽²⁾				

(1) = Expressed in scale units

(2) = Neosynephine® (10%) Winthrop Products Co. Winthrop

(3) = Neosynephine® (2.5%) House Surbiton on the Thames England

(4) = Eppy® (1%) Pharmacia AB Björkgatan 30 Uppsala Sweden

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THERMOGRAPHY IN THE DIAGNOSIS OF DISEASES OF THE EYE AND THE APPRAISAL OF THERAPEUTIC EFFECTS

A Preliminary Report

BY

LILLEMOR WACHTMEISTER

Introduction

In the last 40 years thermography has been increasingly used for industrial and military purposes but only in the last 10 years have a few workers recognised its usefulness in the field of medicine (Lloyd-Williams *et al* 1963 Gershon Cohen *et al* 1965 Bowling Barnes 1965 Notter & Melander 1968)

Every object exchanges energy with its environment and maintains thermal equilibrium with the latter by constantly absorbing and emitting electromagnetic energy such as infrared radiation which is a function of its temperature. Thus every object whose temperature is above absolute zero spontaneously emits and absorbs infra red radiation.

If electromagnetic energy (E) strikes a partly transparent object $E =$ equal to $T + A + R$ T , A and R expressing the object's transmission, absorption and reflexion in per cent. If the object is a mirror E is equal to R and A and T are very small. If the entire object is transparent, T approaches 100 and R and A are small. If the object is opaque E is equal to $R + A$ and T is equal to zero. If the object is opaque with a roughened or blackened surface T is equal to zero R being small and E being equal to A . Absorption of energy

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two eyes in the control group. The results being expressed in scale units. The controls were divided into five groups according to the temperature difference. It is seen that the difference between the two eyes ranged from 0.05 scale units but in a few cases it exceeded 0.5 scale unit.

Fig. 2 shows a histogram of the temperature difference between the right and left eye in the control group. The mean value of the difference is not statistically significant ($P > 0.20$).

Discussion

Pourjafar (1966) observed that the temperature over inflammatory processes and tumours behind the eyeball was elevated in exophthalmos but if the latter was due to other causes it was not elevated. His series included 1 case of carotico-cavernous fistula in which the affected side of the face was cooler than the healthy side. He concluded from this observation that this was due to shunting of blood from the external to the internal carotid artery.

From the observations made in a comparatively large series of cases of mam-

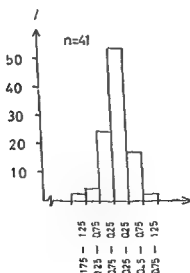


Fig. 2

Histogram of Temperature Difference between the Two Eyes in the Control Group. x coordinate axis shows the difference between the two eyes expressed in scale units. y coordinate axis shows the percentage frequency.

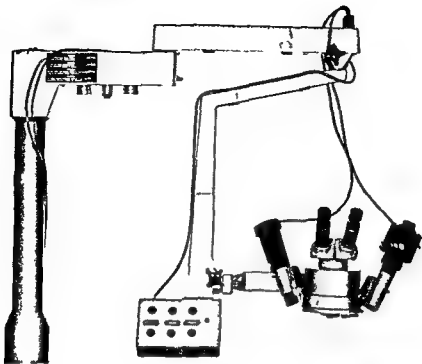


Fig 1

stattet sodass sie auf den leichtesten Fingeraufdruck reagieren Die 3 obersten Knöpfe bewirken dass sich das Mikroskop nach Oben bewegt sowie grossere Vergrösserung und Fokusbewegung aufwärts während die 3 untersten Drucktasten entgegengesetzt wirken Während der Operation ist die Vorderseite der Kassette mit einem sterilen durchsichtigen Plastikstück das mit Heftpflaster befestigt ist zugedeckt

Die Handsteuerung ist für die jüngeren Kollegen eine grosse Hilfe da sie hierdurch mit der Anwendung des Operationsmikroskopes schnell vertraut werden

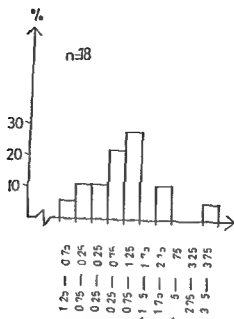


Fig 1

Histogram of Temperature Difference between Affected Eye (Iridocyclitis) and Healthy Fellow Eye

x coordinate axis shows the temperature difference between affected and healthy fellow eye expressed in scale units y coordinate axis shows the percentage frequency

In the case of bilateral central serous retinitis the eye which was more severely affected was warmer by 1.2 scale units than the fellow eye. In the case of panophthalmitis the affected eye was warmer by 0.7 scale units than the fellow eye. On the other hand in the case of episcleritis the healthy eye was warmer than the affected eye.

Table 3 shows the distribution of the difference in temperature between the

Table 3

Temperature Differences⁽¹⁾ between the Two Eyes in the Control Group

Control group	Right eye		No difference	Left eye	
No. of cases 41	> + 0.5	≤ + 0.5	± 0	≤ + 0.5	> + 0.5
Frequency	1	12	12	12	4

(1) = Expressed in scale units

and thermistors photometer (thermal effect) were used but today the leading material is indium antimonide (photoconductive and photovoltaic effect) which is cooled by liquid nitrogen and is sensitive to about 5.5μ . For infrared radiation of longer wavelengths detectors such as germanium (Ge) detectors doped in Hg, Cu or Zn are required. The doped detectors have to be cooled by neon or helium and this is associated with practical difficulties.

For infrared photography IR filters and infrared films are required.

Thermography has been reported to be an important tool to supplement other means of detecting and following up diseases within the fields of plastic surgery, neurology, rheumatology and internal medicine (malignant tumours, burns and vascular diseases).

Whipple reviewed the medical potentials of thermography at the Symposium held in New York in 1964. Pourjat (1966) wrote that the eye was not suitable for examination by the infrared camera (Barnes Model M Thermograph System) available at that time because the temperature gradients were too small, the magnification was insufficient and the scanning time was too long.

Aarts (1969) discussed the applicability of this method to medical problems.

With the exception of Gross *et al.* (1967) and Keeney & Guibor who in 1969 reported at the Conference held at Wills Eye Hospital in Philadelphia on the usefulness of thermography in vascular and malignant diseases of the eye and in other soft tissue pathology, thermography has so far not been used in ophthalmology to the best of author's knowledge.

The recent improvements in the technique of thermography prompted the idea to investigate the value of thermography in the diagnosis of diseases of the eye and the appraisal of therapeutic effects.

Method

Two different types of camera were used: i.e. the * AGA Thermovision® and the Bofors Infrared Camera. Basically both types operate identically but they differ in technical detail. Each instrument has an indium antimonide detector which is cooled by liquid nitrogen and which is sensitive to wavelengths ranging from approximately 1μ to 5.5μ .

The AGA Thermovision® has a shorter scanning time but the optical and thermal resolutions are slightly inferior to those of the Bofors Infrared Camera if theoretical specifications are compared. Both are equipped with a camera unit and a display unit.

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AB Bofors 690, Bofors, Sweden.

many tumours in which thermography enable the differential diagnosis between malignant and benign tumours to be made (Ueland & Notter 1968) Keeney & Guibor (1969) concluded that this should also be possible in cases of tumour of the eye. The latter workers also expressed the view that thermography should enable one to determine whether lesions such as exophthalmos were due to an endocrine disturbance or to inflammatory processes. In the majority of the cases of malignant melanoma and retinoblastoma in their series the affected eye was warmer than the healthy fellow eye.

The thermal picture produced in the thermographs used in this investigation was too small to permit a detailed study of the eye to be made. However, in cases of inflammatory processes in the eyeball and tumours in and behind the eye both instruments proved to be helpful in revealing the condition and appraising the therapeutic effects.

Improvements in some technical features particularly in the magnification of the thermal picture and the thermal and optical performances are required before thermography can be used as a routine method of examination in ophthalmology.

Summary

Thirty eight patients with unilateral or bilateral diseases of the eye were examined by thermography using the AGA Thermovision® and the Bofors Infrared Camera respectively.

Forty one subjects with healthy eyes were identically examined and were used as controls.

It was found that in cases of unilateral acute iridocyclitis, anterior uveitis associated with posterior uveitis, choroiditis, retrobulbar tumour and choroidal tumour the affected eye was on average warmer than the healthy fellow eye.

Improvements in some technical features of the instruments particularly in magnification of the thermal picture and the thermal and optical performances may lead to thermography becoming a useful tool to supplement the current methods used for detecting ocular diseases.

Acknowledgments

Thanks to the courtesy of Messrs AB AGA, Lidö, Sweden, and AB Bofors, Bofors, who kindly made the thermographic apparatuses available to me, it was possible to carry out this investigation. This was of great value to me and I wish to extend my sincerest thanks to them for their generosity and invaluable co-operation.

causes the object's temperature to be increased and this total increase is eliminated through the process of emission as conduction and convection are negligible (*Bowling-Barnes* 1963)

The emission of electromagnetic energy is a fundamental phenomenon in Nature. The total radiant energy (E) emitted by an object is directly proportional to its radiation efficiency factor called emissivity (ϵ) and its absolute temperature (T). This may be expressed by the formula $E = \epsilon T^4 \sigma$ where σ is the Stefan Boltzman constant $= 5.673 \times 10^{-8}$ watt $\text{cm}^{-2} \times \text{K}^{-4}$ (*Bourjat* 1966)

Hardy (1939) demonstrated that human skin emits infrared energy in the wavelengths of approximately 3μ to 30μ with a maximum at about 10μ . He expressed the view that skin may be compared to a perfect emitter called a "black body" whose reflexion and transmission approach zero and peak energy absorption occurs.

The emissivity of human skin, water, plastics and highly polished metallic surfaces in the infrared part of the spectrum has been given to be about 0.99, 0.98, 0.91 and 0.02-0.03 respectively. The radiation efficiency factor is dependent on factors such as the structure and physical characteristics of the object's surface (*Bowling-Barnes* 1963).

The emissivity (ϵ_e) of the eyeball was determined by two different methods in 20 cases: indirectly by estimating the reflexion coefficient (ρ_e) in 10 cases and directly by appraising the emissivity (ϵ_e) in the other 10 cases. According to these preliminary measurements the mean value of the emissivity was 0.9 (0.92-0.99) as determined by the indirect method. There was no noteworthy difference between the eyeball and the skin with respect to emissivity. This also showed that reflexion and the individual differences were negligible.

The corresponding figures as determined by the direct method were 0.8 (0.69-0.89). Thus the danger of extraneous factors influencing the results or misinterpreting the thermal picture can be considered small. Further studies of the emissivity of the eyeball are in progress.

The radiation of heat produces a pattern which can be portrayed by a thermograph. The thermal pattern is influenced by loss of heat, convection, conduction, radiation and evaporation. Thus factors such as vascular and metabolic disturbances and the temperature of underlying structures and pathological processes of the skin also influence the thermal pattern. *Melander & Notter* (1968) have shown that the human body can be chilled to a depth of 3 to 4 cm in an ambient temperature of 23°C and that the chilling increases towards the surface of the body, the temperature gradient being 5°C .

The technique of thermography has been greatly improved in the last few years and different types of detectors have been used, the aim being to shorten the detection time as much as possible without affecting thermal or optical performance. Formerly cholesterol crystals (liquid crystal detector), thermally sensitive phosphors (phosphor effect), differential evaporation (evaporography)

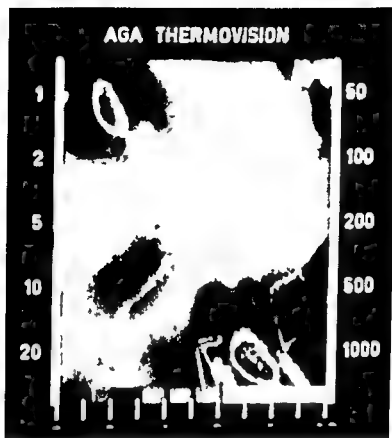


Fig 3

Coloured thermogram AGA Thermovision® derived from a case of iridocyclitis of the left eye. The temperature range was 5°C and the isotherm width about 0.4°C . The violet area in the left upper corner and the dark green area in the lower right corner represent the affected left eye and the healthy fellow eye respectively. The former was 1.0 scale unit warmer than the latter.

Table 1
Comparison of the Technical Features of the ACA Thermovision with those of the
Bofors Infrared Camera

Technical Data	AGA Thermovision® 669	Bofors Infrared Camera
Rotating element	Prism	Mirror drum
Frame rate	16	4
Thermal discrimination Two black body areas at room temperature can be separated	0.2°	0.1-0.2°
Optical resolution	2 mrad 0.3-0.8 mm ²	1.7 mrad 0.25-0.42 mm ²
Number of lines per frame	100	125
Number of dots per line	100	125 (expanded picture)
Sensitivity	20-5.5 μ	1-5.5 μ
Magnification used	1:1	1:2
Distance	0.5 m	0.3 m

each eye of each patient was examined under identical conditions with respect to loss of heat evaporation and any existent air current in the examination room. The ambient temperature ranged from 21° C to 24° C, the relative humidity from 21% to 32% and the atmospheric pressure from 756 mm to 761 mm Hg.

Case Material

This series included 38 patients who were admitted to this Department with the following diagnosis: unilateral acute iridocyclitis (18 cases), anterior uveitis associated with posterior uveitis (3 cases), choroiditis (2 cases), choroidal tumour (5 cases), retrobulbar tumour (2 cases), episcleritis (1 case), panophthalmitis (1 case), contusion of the eyeball associated with iridocyclitis (1 case), tumour of the cornea (1 case), tumour of the iris (1 case) and bilateral central retinitis (1 case).

Vanersborg, Sweden

ANISOMETROPIA AMBLYOPIA
INDUCED ANISEIKONIA AND ESTIMATED CORRECTION
WITH ISEIKONIC LENSES IN 4 YEAR OLDS

BY

W NORDLÖW

The study described in this paper is intended to determine if better final visual acuity in the most ametropic eye in anisometropia is obtained by early correction with isekonic lenses rather than with conventional lenses. If this is the case it will also be shown if a symptom caused by aniseikonia, namely a retarded development of the visual acuity, occurs and a method of treatment would be provided.

Sight testing of 2937 randomly selected 4 year old children comprising 48% of 4 year groups in a representative Swedish population revealed that there was a reduction of visual acuity related to refractive errors in one or both eyes in $64 \pm 0.40\%$. Children with squints were not included in the material. Following full correction with conventional lenses for 3 years $1.33 \pm 0.211\%$ of the children still had a visual acuity of less than 5/5 in one or both eyes. Among the 35 remaining cases there were 19 with anisometropia (with or without astigmatism) of 2 dioptres or more. Among the 139 cases who had a visual acuity of 5/5 there were 2 children with anisometropia of the above amount. The difference is significant ($P < 0.001$) and shows that correction of anisometropia of 2 dioptres or more with conventional lenses, even at the age of 4, does not ensure the development of normal visual acuity. W Nordlöw & S Jouchimsson (1966).

In order to explain the absent or partial improvement of the visual acuity in anisometropia of 2 dioptres or more with full correction by conventional

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- 12 *Aichmair H* Ein verbessertes Instrument zur retrograden Sondierung und Wiederherstellung verletzter Tranenröhrchen Klin Mbl Augenheilk 1967 150 398-400
- 13 *Neubauer H* Grundsätze der Lidchirurgie Klin Mbl Augenheilk. 1965 147 313-335

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ELECTRON MICROSCOPIC DEMONSTRATION OF VIRUS PARTICLES IN HUMAN HERPES SIMPLEX KERATITIS*

**A study with special reference to macroscopically undamaged
areas of the corneal epithelium**

BY

SVEN ERIK G NILSSON

In dendritic keratitis the corneal epithelium generally shows one or more lesions easily recognized in the slit lamp microscope. In severe cases the cells lining such lesions often contain large numbers of newly formed virus particles closely packed to crystalline like bodies. These bodies might be visible in the light microscope as intranuclearly located inclusion bodies. However if only scattered virus particles are present electron microscopy is required for identification.

The ultrastructural features of herpes simplex virus are known from studies of inoculated chorioallantoic membranes and tissue cultures (6, 10, 13, 15, 19) and from experiments using negative staining techniques (20).

Intranuclearly located particles of the same appearance have been demonstrated in electron micrographs of rabbit corneal epithelium inoculated with herpes simplex virus (7, 17, 18). However no systematic studies have been done. An attempt to study human herpetic keratitis was made by Takemura (16). Particles which are likely to be virus particles were seen intranuclearly in the cytoplasm and extracellularly. Due to difficulties in connection with biopsy

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References

- Aarts N J M *Medische Thermographie* (Dutch) Drukkerij Henri Bergmans N V Tilburg Holland 1969
- Aldis A S & Marshall R J *Med & Biol* III 1963 64 p 3
- Backlund E C J *d Electro Radiol* 1967 48 39
- Backlund E C *Experta Medica International Congress Series* No 110
- Baclman Leo J *de Radiol et d Electologie* 1967 48 35 39
- Bjork W J *de Radiol et d Electologie*
- Bourjat P *These pour le Doctorat en Medicine Faculte de Medicine de Strasbourg* 1966 34
- Bowling Barnes R *Science* 1963 140 840
- Bowling Barnes R Gershon Cohen J Brueschke E & Haberman J D *Med & Biol* III 1963 64 175 180
- Brueschke E Haberman Brueschke J D & Gershon Cohen J *Am J of Med Elec* tronic 1965 4 650
- Branemark P J *Spectrum International* 1965 2 26
- Cade M *Ann of the New York Acad of Scien* 1964 121 71 49
- Cade S M & Hanwell E A *Science J* 1966 143 62 67
- Gershon Cohen J Haberman J D *Am U Roentgen* 1965 94 135 740
- Gershon Cohen J & Haberman J D *Monography Recent Advances in the Diagnosis of Cancer* 1966 235 243
- Gershon Cohen J Haberman Brueschke J D & Brueschke E *The Radiol Clinics of North Am* 1965 3 403 431
- Guibor P & Keeney A H *Quoted in Medical Tribune* 20th May 1969 (Unpublished)
- Gros Ch & Vronsoz C *La Presse Medicale* 1966 14
- Gros Ch Bronner A & Vronsoz C *J Radiol Electrol* 1967 43 95
- Hardy J D *J Clin Invest* 1934 13 593
- Lloyd Williams K *Ann of the New York Acad of Scienc* 1964 121 1 and 304
- Lloyd Williams K Cade M C & Goodwin D W *J of Brit inst of Radioengineer* 1963 25 241 250
- Lloyd Williams K Lloyd Williams F & Handley R S *Lancet* 1960 2 958
- Mannsfeld C Bodd G Wallace J Kramer S & Curley R *Radiology* 1968 91 673 678
- Notter G & Melander Q *Fortschritte auf den Gebiete der Roentgenstrahlen und der Nuklearmedizin* 1966 105 657
- Notter C & Melander O *Rontgenblätter* 1968 21 49
- Notter G & Melander O *Electronics in Medicine* 1968 Ljubljana

Table 5

Improvement of vision in 15 anisometropes who used full corrections with conventional lenses and iseikonic lenses for 2-3 years (Group B)

Observation time in years	No. of eyes			Visual acuity									
	Not Examined	Examined											
		Worst	Best	5/5	5/6	5/10	5/15	5/20	5/30	5/40	4 1/20		
0		15*					1	2	4	4	4		
0.5		15				9	2	1	2	1			
1	1	14		1	1	9	2		1				
2		15		2	10	1	1		1				
3	3	12		6	3	2			1				
0		15*	10	2	2				1				
0.5		15	12	3									
1	1	14	13	1									
2		15	15										
3	3	12	12										

* Without correction lens

Zeiss stereo pictures it is known that a certain number have difficulty in appreciating the pictures. This is usually achieved after some practice.

Discussion

Two similar materials of 4 year olds with anisometropia of 2 dioptres or more and representative of a Swedish population have been treated with full correction of the refractive error. Group A and B. Group B has furthermore been given iseikonic corrections estimated for the anisometropia. The visual acuity in this group after three years is significantly better than in Group A. The induced aniseikonia which results from correction of anisometropia with conventional lenses is thus revealed as inhibiting the development of the visual acuity even to the extent of loss of central fixation in some cases. This is thus an objective and measurable sign of aniseikonia. Earlier publications have been mainly concerned with the subjective symptoms of aniseikonia disregarding those cases in which it has been possible to show a measurable improvement of binocular

selected groups of normal cases and patients have been examined. *H F Gillott* (1930 1951) examined 100 specially selected cases in the age groups 8-75 years representative of the population. He found that 42% had aniseikonia of more than 0.8%, and 7% of the group had more than 3%. In 280 Flight Cadets *I M Hicks* (1943) found aniseikonia < 0.5% in 85% and not more than 1% in the remainder. Corresponding results for *H Burian* (1950) among 107 Flight Cadets were 93% and 7%. *P Boeder* (1950) reported that the studies suggest that the frequency of aniseikonia of clinical importance is low.

In order to assess the clinical importance of aniseikonia groups of patients with asthenopic symptoms such as tiredness and headache have been examined. Thus subjective symptoms are involved. The patients have been treated initially with conventional lenses and prisms without or with bad results. After the demonstration of aniseikonia this error has been corrected with an iseikonic lens. *C Berens & M Loutfallah* (1939) obtained improvement of the symptoms in 68% of 418 cases. *I M Hicks* (1943) in 48% of 86 cases. *B Cushman* (1945) in 1% of 24 cases. *J P Macnie* (1948) studied 463 cases and found improvement in 19% after 3 to 6 months and in 50% after 5 to 10 years. *R E Bannan* (1939 1949) and *H F Cillott* (1957) have shown that suppression, poor fusion amplitude and poor stereopsis all objective findings when occurring with aniseikonia can be improved and rendered normal in certain cases by correction with iseikonic lenses.

Furthermore there is one factor to consider in the correction of meridional aniseikonia. There appears in the space eikonometer a measurable declination error which causes erroneous space perception. *A N Ogle & I F Madigan* (1945) *H Burian & A N Ogle* (1945) found that the calculated and observed declination error usually coincided sometimes partly and sometimes not at all. After correction of astigmatism with iseikonic lenses and allowing for the declination error and 9 months to 2 years observation time 85% of 61 cases were more or less improved. The above studies show that asthenopic symptoms with aniseikonia can be abolished or alleviated with iseikonic lenses in 50-80% and binocular vision can be improved in certain cases.

Measurements of aniseikonia in pre school children is not possible with current methods. According to Bannan the children must be at least 6 years of age and have reached sufficient maturity, see at least 20/60 in the worse eye and have binocular vision. *A P Berte & A I Harwood* (1961) consider that children should be older than 6 years, see 6/12 and have binocular vision in order to perform the examination. The Eye Clinic of the Dartmouth Eye Institute introduced the idea that in the absence of the measured value a calculated (empirical) correction of the aniseikonia could be used in the correction of anisometropia (cit *Davis* 1959). This method should be applicable to pre school children to prevent suppression and amblyopia. However there are difficulties in forecasting the degree of aniseikonia in relation to the degree of anisometropia.

vision after iseikonic correction. The results of the examination also indicate that aniseikonia has clinical relevance in the development of visual acuity when it reaches a degree which corresponds to a correction of anisometropia of 2 dioptres or more.

In spite of the fact that all over iseikonic corrections have been used the results have been very good. It probably means that meridional aniseikonia which occurs when astigmatism is corrected is of lesser importance. In Group B the astigmatic difference between the both eyes has been under 2 dioptres in all cases; thus there is no data concerning greater differences. In Group A there were 3 cases with astigmatic differences greater than 2 dioptres. R. J. Davis (1959) proposes that astigmatism in children should always be corrected with estimated meridional iseikonic lenses; should therefore be regarded with certain reservations.

The results from Group A might suggest that it would be reasonable to await the estimation of the visual acuity after half a year of correction with conventional lenses before assessing the prognosis for visual acuity. If a visual acuity of 5/15 is then taken as the upper limit for correction with iseikonic lenses it should be remembered that a few cases with a poorer prognosis may be overlooked. Also valuable time is lost when the development of visual acuity is most amenable to favourable influences. The results of iseikonic correction in this work are the result of starting treatment as soon as the anisometropia has been diagnosed.

Conclusions

1. Full correction of anisometropia of 2 dioptres or more in 4 years olds gives an induced aniseikonia which inhibits the development of visual acuity demonstrable in 2/3 of cases. This is thus an objective result of aniseikonia.
2. An all over iseikonic correction of 0.75-1.25% per dioptre in 4 year olds gives significantly better visual acuity and mitigates against the development of eccentric fixation.
3. Omission of correction with meridional iseikonic lenses of astigmatic differences of less than 2 dioptres between the two eyes seems to be less important.

References

- Ames A. The Space Eikonometer Test for Aniseikonia. *Amer J Ophth* 28: 943 1945
Bannan R. E. Heterophoria and aniseikonia. *Amer J Optometry* 16: 96 1939
Bannan R. E. Aniseikonia and binocular vision. *Amer J Optometry* 26: 240 1949

lenses an induced aniseikonia may be postulated. The resulting difference of size or form of the images of the two eyes could impede the development of visual acuity in the more ametropic and already amblyopic eye. By comparing the results of treatment in the material referred to above with a material collected similarly and derived from the same area of 4 year old anisometropes from other years which also had correction with isekonic lenses it would be possible to assess the importance of aniseikonia in the development of visual acuity.

Review of the Literature

Between the years 1932-1945 Ames and his co workers at the Dartmouth Eye Institute studied in detail theoretically and clinically the differences in size and shape of the images of both eyes. The difference between the images of both eyes which depends on the right and left eye viewing a fixed object from slightly different angles is called physiological. It is necessary for binocular stereoscopic vision. The non physiological difference is called anomalous aniseikonia. It may be optically or anatomically determined. The first may be a function of the factors which determine the refraction of the eye or be induced by correction of refractive errors. Aniseikonia may occur in isometropia. Thus *A. M. Hicks* (1943) found 24 isometropes among 86 cases with aniseikonia. *A. Berte & K. Harwood* (1961) consider that correction of anisometropia is the most common cause to induced aniseikonia. Anatomic aniseikonia may develop for example with varying densities of the sensory cells in the fovea or the cells in the brain.

The difference between the images does not assume any importance until fusion into a conscious picture in the brain occurs. Simultaneous binocular vision is also essential for the diagnosis and measurement of aniseikonia. The apparatus which Ames and his co workers constructed for the measurement was dependent on binocular vision. In the standard eikonometer the relative differences between the images are measured as a percentage. With the space eikonometer the altered spatial perception which is present in aniseikonia is measured. It is averaged and measured as a percentage by means of magnifying lenses. *A. Ames* (1945) and *H. Burian & K. Ogle* (1945) found good correlation of the results obtained by the two eikonometers. The images of different size or form are thus directly related to the subjective change in spatial perception. This is usually not noticed in the everyday environment. It appears in a situation lacking in factors aiding monocular depth perception.

An attempt has been made to find the incidence, degree and clinical importance of aniseikonia. No population study has been made. On the contrary

- Berens C & M Ioutfallah* Aniseikonia - A study of 836 patients examined with the ophthalmic eikonometer *Amer J Ophth* 22 625 1939
- Berte A P & A A Harwood* The Clinical Correction of Aniseikonia *Brit J Physiol Opt* 18 108 1961
- Boeder P* Aniseikonia Theoretical Aspects XVI Concil Ophthal Britannia 1950
- Burian H & A Ogle* Aniseikonia and spatial orientation, *Amer J Ophth* 28 135 1945
- Burian H & A N Ogle* Meridional Aniseikonia at Oblique Axes *Arch of Ophth* 33 293 1945
- Burian H* Aniseikonia Clinical Aspects XVI Concil Ophthal Britannia 1950
- Cushman B* Analysis of cases of aniseikonia *Arch of Ophth* 33 9 1945
- Davis R J* Empirical corrections for aniseikonia in preschool anisometropes *Amer J Optometry* 36 351 1959
- Gilloit H F* The effect on binocular vision of variations in the relative sizes and levels of illumination of the ocular images *Brit J physiol Optics* 13 122 a 215 1956
14 43 1957
- Hicks A M* A Review of 200 consecutive Cases examined on the Eikonometer *Arch of Ophth* 30 298 1943
- Macnic J P* Clinical Aniseikonia *Arch of Ophth* 40 326 1948
- Nordlow W* Accuracy of the Objective and Subjective Method at Determining the Refraction of the Eye *Acta Ophth Scand* 27 349 1949
- Nordlow W & S Joachimsson* Screening Test for Visual Acuity in Four Year Old Children *Acta Ophth Scand* 40 453 1962
- Nordlow W & S Joachimsson* The incidence and results of treatment of reduced visual acuity due to refractive errors in four year old children in a swedish population *Acta Ophth Scand* 44 152 1966
- Ogle A N & L F Madigan* Astigmatismus at oblique axes and binocular stereoscopic spatial localization *Arch of Ophth* 33 116 1945

than the skiascopic value. Astigmatism of up to 2 dioptres has been fully corrected. Higher astigmatism has been under corrected initially. In some cases smaller changes in the spectacle corrections have been made during the period of treatment as indicated by the visual acuity and the corneal astigmatism as measured by the ophthalmometer. In addition to this treatment, some of the material (Group B) has been given an all over isekonic correction of 0.75-1.25% per dioptre of anisometropia. The cases have been assessed about 0.5-1st and 3 years after the beginning of treatment.

Material

As previously mentioned in the Introduction the material was composed of 49% of 4 year olds from each of several year groups from the same geographical area. It has been collected through sight testing W. Vordlow & S. Joachimsson (1966) and is representative of the Swedish population. Of these 4 year olds those with anisometropia of 2 dioptres or more have been made the subject of this study. Anisometropia of this degree occurs in $0.72 \pm 0.15\%$ of 4 year olds. The degree of anisometropia is defined as the difference between the two most hypermetropic principle meridians in hypermetropia or the two least myopic principle meridians of both eyes in myopia. At astigmatism of unequal degree the difference in the other principle meridians is another. The material can be divided into two groups with respect to treatment.

A Correction with conventional lenses and

B Even magnifying correction isekonic lenses

Group A comprises in addition to the anisometropes which were described in 1966 by Vordlow & S. Joachimsson and were born between 1954 and 1960 inclusive also those born between 1957 and 1959 inclusive thus in all seven year groups. They include a total of 31 cases. From these were removed two who had moved away from the area, one who failed to attend and two who received isekonic correction during the period of treatment. These five cases did not differ from the remainder concerning the results of the initial examination. Thus there remain 32 cases in this group.

In Group B are those anisometropes born between 1960 and 1962 inclusive thus from three year groups. The group consists of 15 cases.

As has been mentioned the sight testing was performed during the fourth year of life. Because of some delay in examination and refraction in the eye reception the spectacle correction has been delayed. Some have reached the age of five years (Table 1).

The refractive errors are shown in Table 2. In group A the anisometropia varied between 2 and 7 dioptres. Uncomplicated anisometropia, the same dif-

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CAROTID CAVERNOUS FISTULA WITH CONTRALATERAL EXOPHTHALMOS

BY

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A fistula between the internal carotid artery and the cavernous sinus is usually caused by trauma but may result from spontaneous rupture of an aneurysm as a rule an arteriosclerotic one. Irrespective of the pathogenesis arterial blood will be shunted in retrograde direction from the cavernous sinus into the superior ophthalmic vein. This results in exophthalmos which may be pulsating and in engorgement of superficial and retinal veins. Other symptoms such as frontal pain, pulse synchronous noises in the head and palsies of ocular muscles may occur.

Usually the exophthalmos appears on the side of the fistula but simultaneous or subsequent involvement of the opposite orbit is common due to the presence of connections between the cavernous sinuses on both sides.

The exophthalmos may be mainly or exclusively contralateral. This is a rare finding as demonstrated by the fact that in reports on this phenomenon each author has presented only one case of his own. In this paper the literature will be reviewed and a new case in which the mechanisms were elucidated by carotid angiography will be reported.

Review of the literature

The literature contains detailed reports on 11 cases of carotid cavernous fistula with mainly contralateral exophthalmos. The principal data are collected in Table 1.

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In 30 % of the cases agreement is good in 40 % less good and in 30 % there is no aniseikonia according to Ogle (cit Davis 1959) R J Davis (1959) considers that with pre school children it is better to treat with an estimated aniseikonic correction than with none at all Bannon suggests approximately 1 % and Ogle 1.5 % magnifying for each dioptre of anisometropia Davis believes that at present it is best to correct the total meridional error irrespective of the position of the axes There does not appear to be a published study of the results of applying the estimated aniseikonic correction in anisometropia in pre school children

Method

The visual acuity has been measured at the screening examination and in more detail in the Eye Department with Bostrom Marques Squares according to the method of W Nordlow & S Joachimsson (1962) The angular visual acuity is measured The visual acuity has been recorded as the smallest square the opening of which has been given correctly four times in succession This value has been used to compare the results of examinations on different occasions

To obtain an idea of how the visual acuity as measured above agrees with the method using letters in rows according to Monoyer both methods have been used when the children have reached the age of 8 years With the latter method recognition and ability to separate are both involved It was found that of 350 consecutively tested eyes with refractive errors and reduced visual acuity which improved on treatment to 5/5 294 had visual acuity 1.0 49 had 0.9 5 had 0.8 and 2 had 0.7 If allowance is made for the error of the method in comparing the two methods at ± 0.1 98 % show complete agreement

The refraction was determined by skiascopy (stigmatoscopy) after atropinisation for 3 days (1 % Atropine Sulphate solution twice daily) A point source of light has been used the light from which has been projected into the eye with a plane parallel glass The examination distance has been 0.5 metres The relation between the skiascopic value and the optical condition of the eye in accommodation rest has been calculated previously W Nordlow (1949)

The fixation of the worse eye has been assessed in some cases by means of the visuscope

Binocular function has been assessed on the synoptophore The balance has been assessed using the spider and net for the fusion amplitude L and F (8×6 mm) have been used and for stereopsis photocopies of Zeiss test objects with silhouettes for the Zeiss stereoscope Examination of stereoscopic vision has been confined to the preliminary test and picture 5

The whole material has been given spectacle correction of 0.5 dioptres less

Table 1
Clinical data of 13 cases of carotid cavernous fistula with contralateral exophthalmos

Author(s)	Sex Age	Origin	A Ipsilateral ocular signs	B Contralateral ocular signs (in add to exophthalmos)	Interval between A and B	Carotid compression test	Angiography
Reif (1899)	f 25	traumatic	palpable pulsation paresis N III and VI	palpable pulsation papilloedema	0	+	no
Pincus (1907)	m 31	traumatic	optic atrophy paresis N III IV and VI	palpable pulsation paresis N VI	7 weeks	+	no
Dandy & Follis (1941)	m 53	traumatic	exophthalmos optic atrophy paresis N III and VI	visible pulsation optic atrophy paresis N VI	0	+	no
Ramos & Mount (1953)	f 54	traumatic	none	ptosis paresis N VI		—	yes
Tamler (1954)	m 86	spontaneous	paresis N III and VI	paresis N III and VI	2 months	+	yes
Graelcau & Namin (1954)	f 67	spontaneous	none	papilloedema retinal haemorrhages paresis N III		?	yes
Kunc & Dulik (1954)	m 31	traumatic	none	visible pulsation paresis N VI		+	yes
Rouviès & Rouviès (1955)	m 21	traumatic	none	total ophthalmoplegia		+	no

Table °
The refractions of 47 anisometropes at the start of treatment

The refractions of 47 anisometropes															Case difference in astigmatism between right and left eye																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																												
Group	No		Refraction						Anisometropia in dioptres						Eye degree of astigmatism in dioptres																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																												
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Walsl (1957)	m 43	traumatic?	paresis N VI	corneal hypaesthesia paresis N III and VI	0	+	?
White et al (1955)	f 49	traumatic?	none	visible pulsation paresis N III and VI		+	yes
David et al (1964)	m 34	traumatic	optic atrophy	papilloedema	5 months	+	yes
Girard et al (1966)	m 45	traumatic	paresis N VI	external ophthalmoplegia	9 weeks	+	yes
Graham (1966)	f 64	traumatic	paresis N VI	visible pulsation paresis N VI	A 9 months after B	+	yes

Table 1
Age distribution of 47 anisometropes at the beginning of treatment

Group	No of cases	Age in years when corrected							
		With conventional lenses				Also with iseikonic lenses			
		4-4.5	4.5-5	5-5.5	5.5-6	4-4.5	4.5-5	5-5.5	5.5-6
A	32	5	21	5	1	—	—	—	—
B	15	2	7	5	1	2	6	5	0

ference between all meridians in both eyes occurred in 12 cases. In the other 20 cases there was also astigmatism with a difference of 0.35 dioptres between both eyes. In 18 of 32 cases the anisometropia was between 2 and 3 dioptres and in 10 of 20 cases the astigmatic difference was less than 1 dioptre. The refractive errors in Group B did not differ from those in Group A.

With iseikonic correction of astigmatism with oblique axes there is a so-called declination error as has been referred to in the review of the literature. It is therefore of interest in this connection to see how frequently oblique axes occur in a representative group of anisometropes (A and B). A deviation greater than $\pm 10^\circ$ from vertical or horizontal axis occurred in 8 cases out of 29 of the worst eyes and in no cases out of nine of the best eyes.

Results

Group A (32 cases) With regard to the change of anisometropia it may be mentioned that it remained unchanged during the period of observation in 15 cases. It reduced by 0.5-1.5 dioptres in 15 cases, 2.5 dioptres in one case and increased in one case. In only three cases the anisometropia reduced to less than 2.0 dioptres.

The visual acuity could be measured at the first examination in 31 cases and varied in the worst eye from 5/15 to 1/50 without correction. After 3 years of correction with conventional lenses it had improved to a greater or lesser extent in all cases (Table 3). A good visual acuity 5/5 and 5/6 was achieved in 12 eyes. In explanation it can be proposed that only a slight or absent induced aniseikonia was present. In 10 eyes a visual acuity of 5/10 and in 10 eyes 5/15 or 5/30 was achieved, thus poor results. One can say that 1/3 of the cases responds

It should be added that one case was reported by Velpeau as early as 1839 as briefly mentioned by Pincus (1907) Schirmer (1898) described another case that seems to have been identical to that of Reif (1899) Jefferson (1950) reported on one case in an unpublished lecture Furthermore one case was briefly mentioned by Taveras & Wood in their textbook of *Diagnostic Neuroradiology*

Bilateral ocular changes were present in 8 of the 13 cases In 7 the contralateral exophthalmos appeared simultaneously with the ipsilateral changes or after an interval of two weeks to three months but in the case of Graham (1966) the ipsilateral sixth nerve paresis appeared later than the contralateral exophthalmos In the case of Dandy & Follis (1941) the ipsilateral exophthalmos had disappeared after several years and the clinical picture was dominated by the contralateral exophthalmos Exclusively contralateral changes existed in 5 cases Visible or palpable pulsation of the bulb was noted in 6 cases

The patient often describes pulse synchronous noises in the head which can readily be heard with a stethoscope The bruit may be eliminated by compression of the carotid artery in the neck on the same side as the fistula but not by compression on the other side This examination often incorrectly called Matas test was positive in at least 11 of the 13 cases Only in the case of Ramos & Mount (1953) was the test negative due to the fact that the fistula was largely supplied by the vertebral arteries

A prerequisite for the development of ipsilateral exophthalmos is a free communication between the cavernous sinus and the superior ophthalmic vein The cause of a blockage is proposed by Reif (1899) to be a thrombosis of the superior ophthalmic vein In the case of Dandy & Follis (1941) an occlusion of the ipsilateral vein was verified at autopsy In the case of Tamler (1954) also examined at autopsy no ophthalmic vein could be found entering the cavernous sinus Ramos & Mount (1953) and several subsequent authors found no communication between the ipsilateral superior ophthalmic vein and the cavernous sinus at angiography Tamler (1954) suggested that this lack of communication might be due to one of several conditions e.g. a thrombus or a traumatic rupture of the vein an obstruction of its proximal portion by a dilated carotid artery or an anomaly of its course

Case report

A D a man aged 74 had previously been treated for myocardial infarction One night he woke up with an intense frontal headache Three hours later it had diminished but not disappeared In the morning he also complained of double vision Two days later he was examined by an ophthalmologist who found paresis of the medial rectus the palpebral levator and the pupillary sphincter of the left eye, but no other signs

Table 4

Type of fixation in 19 of 32 anisometropes who had correction with conventional lenses for 3 years (Group A)

Worst eye		Type of fix	Final visual acuity					
Examined	No		5/5	5/6	5/10	5/15	5/20	5/30
Yes	15	f		4	10	1		
Yes	4	pf				3	1	
No	13		3	5		3	1	1
Total	32		3	9	10	7	2	1

f = foveolar

pf = para foveolar

($P < 0.001$) A half year visual acuity of 5/15 or less indicates a poorer response to treatment with conventional lenses

Group B (15 cases) The anisometropia remained unchanged during the period of observation in 7 cases reduced by 0.5-1.5 dioptres in 6 cases and increased 1-2 dioptres in 2 cases. A reduction to less than 2 dioptres occurred in one case. The agreement with Group A is good.

As in Group A the visual acuity was 5/15-1/30 in the worse eye at the first examination. After using isekonic correction in 12 cases for 3 years and in 3 cases for 2 years the visual acuity was 5/5 in 6 cases and 5/6 in another 6 cases i.e. good in 12 cases. In 2 cases the visual acuity became 5/10 and in one eye 5/30 (Table 5). Thus poor visual acuity occurred in one case out of 15 against 10 cases out of 32 in Group A. On testing with the χ^2 test it was revealed that a visual acuity of 5/5 and 5/6 was obtained significantly more often with isekonic lenses than without ($P < 0.01$).

With regard to the type of fixation in the worse eye at the first examination in Group III of 14 cases examined 12 had foveolar fixation and 2 parafoveal fixation. At the final examination one of the 14 cases still had parafoveal fixation (visual acuity 5/30). The child whose fixation had not been tested at the first examination had foveolar fixation at the final examination. Parafoveal fixation was thus present in one case out of 15 corrected with isekonic lenses against 5 cases (4 definite) out of 32 without such correction.

Binocular vision was examined in 14 cases. Of these 13 had N.R.C. and fusion amplitude. The fourteenth case had parafoveal fixation and suppression. With regard to stereopsis 13 cases managed the preliminary test and 7 cases picture 5 also. As it was the first time the children had performed this test the result may be regarded as a minimum value. From examination of adults with

The next day the ptosis and the mydriasis had increased. The patient was referred to the Department of Internal Medicine at the local hospital where he was treated as an inpatient. The headache was of moderate intensity and located around the left eye. General and neurological examinations were negative except for the ocular findings. The blood pressure was 170/95. Bilateral carotid angiography one week after the appearance of the symptoms disclosed a carotid cavernous fistula on the left side and a retrograde filling of the superior ophthalmic vein on the right side.

The following day the patient noticed a swelling of his right eye. At ocular examinations the eye lids and conjunctiva of the right eye were found to be swollen and the conjunctival and retinal veins engorged and there was a right sided exophthalmos of 9 mm. No pulsations of the bulb were observed but a pulse synchronous bruit was heard over the temporal regions. The left oculomotor paresis was unchanged. Later the corrected visual acuity of the right eye was found to decrease successively from almost normal to 0.4.

Due to this progressive course he was taken into the Department of Neurosurgery University Hospital Lund. During his stay in this hospital the intensity of the headache varied and he was sometimes disturbed by a noise in his head. General and neurological examinations were still normal except for the ocular findings.

Ocular findings

Visual acuity finger counting 1 meter R.E. 0.7 L.E.

Perimetry concentric contraction right field. Normal left field.

Ocular tension normal both eyes.

Hertel 25 mm R.E. 15 mm L.E.

R.E. non pulsating exophthalmos. Total ptosis + external and internal ophthalmoplegia. Hyperaemia and oedema of eye lids and conjunctiva. Corneal hypaesthesia. Keratitis with oedema and epithelial defects. Slight papilloedema and dilated retinal veins. L.E. slight ptosis and paresis of the medial rectus. Normal pupil. Senile degeneration of the macula.

A pulse synchronous bruit was heard over both frontal and temporal regions. It ceased at compression of the left common carotid artery but not of the right.

Bilateral carotid angiography

The carotid arteries and their branches were tortuous and widened and multiple arteriosclerotic irregularities were present. As in the previous examination there was a shunting of blood from the left carotid artery to the cavernous sinus and to the right superior ophthalmic vein. The width of the latter vessel had increased. There was still no filling of the left superior ophthalmic vein. (Figs. 1a-c)

During the week following the angiographic examination the headache and the bruit disappeared and the exophthalmos began to decrease. Due to this spontaneous improvement no operation was performed and he was discharged to his local hospital. Later there was regression of the keratitis and improvement in vision. Six months after the onset of his illness the visual acuity of the right eye was 0.5 and the exophthalmos was only 1.5 mm. The cornea was normal. There was still a slight paresis of the right medial rectus muscle.

A month later the patient had acute abdominal pain, caused by an aneurysm of the

Table 3

Improvement of vision in 32 anisometropes who had full correction with conventional lenses for 3 years (Group A)

Observ time in years	No of eyes			Visual acuity								
	Not Examined	Examined										
		Worst	Best	5/5	5/6	5/10	5/15	5/20	5/30	5/50	4 1/50	
0	1	31*					4	6	8	5		8
0.5	4	33			5	6	8	4	4			1
1	0	32			7	11	4	5	4	1		
2	2	30		3	7	13	5		2			
3	0	32		3	9	10	7	2	1			

0	1	31*	17	7	6	1						
0.5	4	28	20	7	1							
1	1	31	27	4								
2	2	30	27	3								
3	0	32	31	1								

* Without correction lens

well to the treatment and that an induced aniseikonia may have prevented the development of full visual acuity in the remaining 2/3. The type of fixation was examined in 19 cases (Table 4). It was found that 4 cases lacked foveolar fixation. It was suspected that a further 4 cases belonged to this group which thus represents a quarter of the total. It may be considered as an unexpectedly high frequency to ascribe to the aniseikonia.

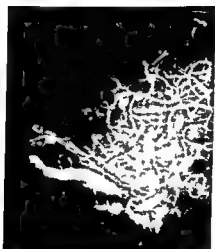
It would of course be valuable if it could be decided at the beginning of treatment which cases would have poor visual acuity and then start with isekonic lenses. After scrutiny of the initial visual acuity, the degree of anisometropia and astigmatism in correlation with the final visual acuity and testing with the χ test, no guidance is obtained concerning the importance of these factors. On the contrary, it shows that the visual acuity obtained after the wearing of a spectacle correction for half a year is a more certain parameter for assessing the prognosis. It is of course a test of the response of the eye. Of 19 eyes with a half year visual acuity of 5/15 or less, 3 obtained a visual acuity of 5/6 or better and 16 a visual acuity of 5/10-5/30. Of 13 eyes with a half year visual acuity of 5/10 or better, 11 achieved a visual acuity of 5/5 or 5/6 and 2 a visual acuity of 5/10. The χ^2 test shows that the difference is significant.



1a



1b



1c

Figs 1a c

Left sided carotid angiography showing a left sided carotid cavernous fistula and a filling of the superior ophthalmic vein on the right side but not on the left

abdominal aorta This was treated surgically but six days after the operation he suddenly died from a second myocardial infarction At post mortem the cavernous portion of the left internal carotid artery was found to be dilated and there was an advanced arteriosclerosis of the basal cerebral vessels The orbital vessels were not examined

Comments

In the reported case the carotid cavernous fistula was of the so called spontaneous type It occurred in an old man who was subject to several arterio

Table 4

Type of fixation in 19 of 32 anisometropes who had correction with conventional lenses for 5 years (Group A)

Worst eye		Type of fix	Final visual acuity					
Examined	No		5/5	5/6	5/10	5/15	5/20	5/30
Yes	15	f		4	10	1		
Yes	4	pf				3	1	
No	13		3	5		3	1	1
Total	32		3	9	10	7	2	1

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sclerotic diseases and who ultimately died from myocardial infarction following an operation for an aortic aneurysm

The initial ocular signs were slight and located to the side of the fistula. After one week they were accompanied by a pronounced contralateral exophthalmos. In combination with trigeminal involvement this resulted in a keratitis with visual deterioration. Eight weeks after the onset of symptoms a spontaneous regression of the ocular changes started.

As in almost all the other similar cases reported by previous authors the carotid compression test was positive and found to be valuable for the determination of the side location of the fistula.

The absence of ipsilateral exophthalmos is in accordance with the angiographic finding of no communication between the cavernous sinus and the superior ophthalmic vein on that side. This is in agreement with the observation of Dandy & Follis (1941), Ramos & Mount (1953), Tamler (1954) and other previous authors. In our opinion the most probable explanation is that there was a thrombosis in the superior ophthalmic vein. In our case a lack of communication due to vascular abnormalities seems unlikely.

Summary

Cases of carotid cavernous fistula with mainly or exclusively contralateral exophthalmos are rare. This paper contains a review of the literature concerning these cases and a report on another case.

The exophthalmos is caused by an engorgement of the orbital veins. The absence of ipsilateral exophthalmos in our case and in most of the previously reported cases was probably due to a thrombosis in the superior ophthalmic vein blocking the passage to the veins in the orbit.

References

- Dandy W E & Follis R H (1941) On the pathology of carotid cavernous aneurysms (pulsating exophthalmos). *Am J Ophthalm* 34 (1941) 315-335.
David M, Metzger J, Mikol F & P. Pradat (1964) Fistule carotido-caverneuse avec exophthalmie controlatérale. *Neurochirurgia* (1964) 36-93.
C. and P. F. Boucher M. Allegre C. Leclerc F & M. Bochu (1966) Fistule carotido-caverneuse à expression ophtalmologique controlatérale. *Confinia neuro* 23 (1966) 2-6.
C. and P. F. Boucher M. Allegre C. Leclerc F & M. Bochu (1966) Anévrysme artérioveineux carotido-caverneux spontané à symptomatologie oculaire uniquement controlatérale. *Rév neuro* 91 (1964) 303-310.

technique and embedding technique the tissue preservation obtained in this material was not of a quality permitting a more precise analysis however

In superficial dendritic keratitis the lesions are generally well defined and well demarcated. As judged from examination in the slit lamp microscope the remaining areas of the corneal epithelium look undamaged at least at early stages of the disease. One thus gets the impression that the infection is restricted to the lesions. The present electron microscopic investigation was undertaken in order to establish whether or not signs of infection with virus could be found in the cells of the clinically undamaged areas of the corneal epithelium. It appears that the results of such a study would be of interest as to the therapeutical measures in dendritic keratitis as well as to the question of recurrence of the disease.

Materials and Methods

Two young men both having a history of dendritic keratitis four and six years ago respectively were examined two days after the onset of symptoms of the first recurrence. Upon examination in the slit lamp microscope lesions typical of dendritic keratitis stained with fluorescein were seen in the corneal epithelium. In one of the cases herpes simplex virus was also identified by means of isolation and serological tests. Strips of clinically undamaged corneal epithelium located two to five mm away from the closest lesion were carefully removed from the cornea under visual control in the slit lamp microscope. A spud designed for removal of corneal foreign bodies was used for the dissection. Strips containing a lesion were also removed. All strips were immediately immersed into cold 1% osmium tetroxide fixative buffered with Veronal acetate and made approximately isotonic with plasma. After dehydration in acetone the tissue was embedded in Vestopal W. The sections subsequently stained with uranyl acetate and lead citrate were examined in a Siemens Elmiskop I which was kindly put at my disposal by prof. H. Thorell, Department of Pathology, Karolinska Sjukhuset, Stockholm.

Results

The cells of the necrotic tissue lining the active dendritic lesions contained large numbers of virus particles morphologically identical with herpes simplex virus. This finding was expected and will not be dealt with in detail here.

All micrographs of the present investigation were taken of clinically intact

Survey picture of superficially located cells of human corneal epithelium. This micrograph as well as the following micrographs were taken of clinically intact corneal epithelium located two to five mm away from the closest visible lesion in dendritic keratitis $\times 9,000$

Fig 1



cornel epithelium located two to five mm away from the closest visible lesion. A survey picture of some cells from one of these biopsies is shown in Fig 1. At this magnification the cells appear normal. At somewhat higher magnification intranuclearly located structures with an appearance similar to herpes simplex virus could be found in the great majority of the cells investigated however (Figs 2 and 4). The number of virus particles per cell was fairly small compared to that of the cells lining the lesions. The virus particles were often located close to electron dense areas in the nucleoplasm. An intranuclearly located virus particle (or virion) consisted of an inner core and an outer capsid (Figs 3 and 5). The core which is the DNA contain ing part of the virus particle was generally spherical or slightly oval. Its center was in most cases less opaque than its periphery. This was evident particularly

- Graham M V* Arterio venous shunt in the cavernous sinus with contralateral ocular signs *Brit J Ophth* 50 (1966) 599 602
- Kunc Z & F Dulík* Carotid cavernous aneurysm with contralateral pulsating exophthalmos *Čsl Oftbal* 10 (1954) 30 36
- Pincus F* Spontanheilung eines traumatischen pulsierenden Exophthalmus *Ztschr f Augenheilk* 13 (1907) 33 41
- Ramos M & L A Mount* Carotid cavernous fistula with signs on contralateral side. *J Neurosurg* 10 (1953) 178 182
- Reif E* Ein Fall von doppelseitigem hauptsächlich gekreuztem pulsierendem Exophthalmus *Beitr z Augenheilk* 4 (1899) 545 562
- Rouves L & C Rouves* Etude EEG d'un cas d'anévrysme carotido-caverneux post-traumatique a symptomatologie oculaire controlaterale *Rév neurol* 93 (1955) 456-493
- Tamler E* Carotid cavernous fistula with typical signs on contralateral side only *Arch Ophth* 52 (1954) 433 441
- Tavernas J M & E H Wood* Diagnostic Neuroradiology Baltimore Williams & Wilkins Co (1964) 1960 pp
- Walsh F B* Clinical neuro ophthalmology, Baltimore Williams & Wilkins Co (1957) 1294 pp
- White J C, Love J G & N P Goldstein* Carotid cavernous fistula on left side with ocular symptoms on right side *Proc Staff Meet Mayo Clin* 33 (1958) 441 445

prisms was rotated 90° , in order to present an image rotated 180° to one of the eyes (Fig 2 and 3) The displaced part of the square wave gives the transverse disparity necessary for the perception of stereopsis and the observer just has to determine whether the middle segment of the target is situated in front of the reference lines or behind them It must be observed that with this method of producing a stereo situation the pupillary distance is of no importance

The two disparate images so produced are easily "fused" by most observers with normal bifoveolar fixation The sum of the vernier off sets - the stereo disparity - must of course be within the limits of Panum's zone and the test object on the oscilloscope screen must be symmetric with regard to a vertical plane in the center of the target

By means of this prismatic device any type of heterophoria of the observer's

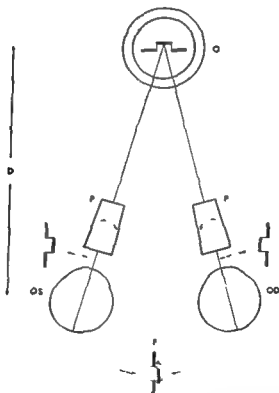


Fig 3

Schematic illustration of the method by which a stereoscopic situation is produced By means of a prismatic device (P) the images of the square wave on the oscilloscope (O) are rotated clock wise for the left eye and counter clock wise for the right eye When the images are fused a transverse disparity is produced The displaced segment of the target is perceived either in front of or behind the plane of the reference lines depending on the direction of the displacement (a)

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OBSERVATIONS ON VERNIER AND STEREO ACUITY WITH SPECIAL REFERENCE TO THEIR RELATIONSHIP

BY

GÖRAN STIGMAR

Introduction

The vernier and stereo visual functions are in many respects very closely connected as noted by many authors (*Links 1952 Ludvig 1953 Le Grand 1956* and others). Both are said to be based on the perception of relative direction differences (*Ludvig 1953*).

Vernier acuity (nonius acuity or aligning power) is the ability to detect a break in a contour or irregularity in a line. As pointed out by *Ludvig & Bair (1953)* a distinction must be made between the perception of relative direction differences in a vernier or a stereoscopic situation and the perception of the absolute location of an object in space a fact which makes the traditional terms direction (or localization) sense of the eye inappropriate names for this capacity of the visual system.

Stereoscopic vision is in this investigation only studied within the limited range of binocular vision which *Ogle (1952)* has defined as the region of patent stereopsis. The stereoscopic acuity in this range has an accuracy comparable with the vernier acuity.

It has been almost generally accepted that the disparity (transverse disparity) between the retinal images is the only stimulus necessary to release the perception of stereopsis. This conception was stressed not least by *Ogle (1959)*.

eyes can be compensated. This can be accomplished by changing the position of the axes of the prisms. With two micrometer screws the prism axes are most carefully adjusted with regard to the optic axes of the eyes.

(4) Monocular and binocular vernier functions

From experiences with the stereo vernier situation it seemed logical to study also the monocular versus the binocular vernier function.

The examination of monocular and binocular vernier performances was carried out in principally the same way as previously described. In a random way the subject had to interpret a vernier pattern (target Type A) with its different separation distances monocularly or binocularly. In order not to produce a change of the size of the pupil in the monocular situation by occluding the contralateral eye a diffusing filter was placed in front of that eye. Three experienced subjects took part in the examination.

III Experimental arrangements

Throughout the various experiments all parts of the arrangement were kept constant. The illumination of the room (of about 15 lux) the luminance of the test object and the background illumination on the oscilloscope screen were chosen to give optimal viewing comfort and visual acuity. In some of the experiments a background target consisting of concentric circles was used as a stimulus for fusion. During the course of the experiments however it turned out to be unnecessary to use this fusion stimulating background since all the experiments were made in an orthophoric state of binocular vision. It was found that the reference lines (r) alone were a stimulus for fusion strong enough to maintain a stable bifoveolar vision throughout the examination session.

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The subject was placed 5 m in front of the test object viewing the target through the prismatic device. Uniformly illuminated unstructured screens with small apertures restricted the binocular field allowing nothing else but a field subtending 8° around the test object to be seen by the observer. Due to the rotating effect of the prisms it was necessary to have a neutral surrounding visual field.

Each experimental session consisted of a stereo vernier block of 10 min (Fig. 4) 5 min for each situation starting with one of the targets presented either in the vernier or stereo situation in a random way. The maximum expo

- Graham M V* Arterio venous shunt in the cavernous sinus with contralateral ocular signs *Brit J Ophth* 50 (1966) 599 602
- Kunc Z & F Dulik* Carotid cavernous aneurysm with contralateral pulsating exophthalmos *Csl Ophthalm* 10 (1954) 30 36
- Pincus F* Spontanheilung eines traumatischen pulsierenden Exophthalmus *Ztschr f Augenheilk* 18 (1907) 33 41
- Ramos M & L A Mount* Carotid cavernous fistula with signs on contralateral side *J Neurosurg* 10 (1953) 178 182
- Reif E* Ein Fall von doppelseitigem hauptsächlich gekreuztem pulsierendem Exophthalmus *Beitr z Augenheilk* 4 (1899) 545 562
- Rouves L & C Rouves* Etude EEG d'un cas d'anévrysme carotido caverneux post-traumatique a symptomatologie oculaire controlatérale *Rév neurol* 93 (1955) 486 493
- Tamler E* Carotid cavernous fistula with typical signs on contralateral side only *Arch Ophth* 52 (1954) 433 441
- Taveras J M & E H Wood* Diagnostic Neuroradiology Baltimore Williams & Wilkins Co (1964) 1960 pp
- Walsh F B* Clinical neuro ophthalmology Baltimore Williams & Wilkins Co (1957) 1294 pp
- White J C Love J G & N P Goldstein* Carotid cavernous fistula on left side with ocular symptoms on right side *Proc Staff Meet Mayo Clin* 33 (1958) 441 445

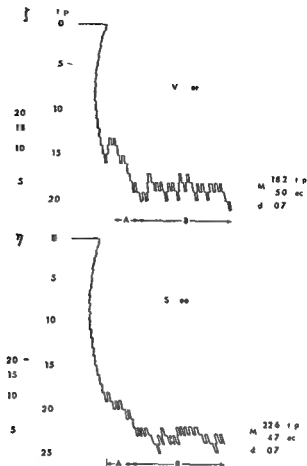


Fig 4

A stereo vernier block as it appears from the recorded graphs. A illustrates the adjustment period and B the 4 minute period which is the base for the mean value calculations. In the illustrated recordings there are no significant differences between vernier and stereo thresholds.

sure time for each interpretation was 4 sec with short intervals of 0.5 sec. Most observers made use of only about 2 sec of exposure time, thus having time for about 150 trials during a 5 minute period (right or left in front of or behind). Each block was followed by a pause. No subjects were required to have more than three sessions in any one day.

Definitions

Most of the symbols are indicated in Fig. 1.4. The offset of the oscilloscope line is designated a , which gives a retinal displacement a' . If the observation

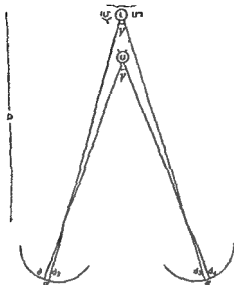


Fig 1

Two dimensional illustration of a stereo vernier situation as seen from above modified after Walls. The test object consists of two rods (L and U) vertically arranged. In the vernier situation the upper rod is either to the right or to the left of the lower rod and the dislocation (a) between them gives rise to the different visual directions (d_1, d_2) with a displacement (a) in each eye. If the upper rod is placed in front of (or behind) the lower rod in the intersection of d_1 and d_2 and the resulting transverse disparity (a) is small a stereoscopic situation is given with the same monocular disparity. In this investigation a vertically arranged three rod test was used as a target and the change from the vernier situation to the stereoscopic one was accomplished by a prismatic device giving an identical test situation for the testing of both acuities. The

$$\text{angle of disparity } (\gamma) \approx \gamma - \gamma' = \frac{2a}{D}$$

that the stereo acuity was not as much affected as the vernier acuity when the separation distance was increased. Berry concluded the stereoscopic thresholds were for the most part too low to be accounted for by a simple summation of the two separate monocular vernier components. Thus he found stereoscopic thresholds between 2.4 sec and vernier thresholds between 3.7 sec in three subjects within a certain range of separation differences between the rods.

Method

With a new automatic technique described by Arakau (1967a) using a square wave on an oscilloscope as the same test object for both the vernier and the

distance $\equiv D$ (from the nodal point of the eye to the fixation point) the angle subtending the off set $\equiv \frac{a}{D}$ (radians)

In the vernier situation the retinal displacements (a) in both eyes have the same direction and the vernier off set is defined by $\zeta = \frac{a}{D}$. In the stereo situation the retinal displacements are in opposite directions and the angular disparity of the two off sets then will be $\eta = \frac{2a}{D}$. The thresholds of vernier and stereoscopic perception ζ_t and η_t are obtained from the recorded graphs (Fig. 4) and they are expressed in terms of $\frac{a_t}{D}$ and $\frac{2a_{st}}{D}$ where a_t denotes the threshold vernier off set and $2a_{st}$ the threshold stereo disparity. As statistical quantities they will be discussed in the following section.

Material

(a) Observers

Five experienced observers served as subjects. Their corrected visual acuities according to Monoyer's letter chart were 1.0 or more on both eyes. Refraction varied from +0.5 to -2.0. In order to eliminate the training effect - which is a striking fact in vernier acuity as well as in stereoscopic acuity - the subjects were previously trained in several sessions. Then the observers had reproducible threshold values for both functions.

(b) Evaluation of the records

Every experimental examination started with the test object on "step 0" where the vernier off set was 2 mm ($\frac{2a}{D} \approx 83$ sec arc). After three correct interpretations the test object corresponding to step 1 was presented ($a_1 = \frac{2a}{1.25}$) and in the same way the following steps were automatically presented for interpretation by the subject. Thus a step curve was recorded indicating the number of transitions from one step to another during a 5 minute period.

Two parts of each curve can be identified. The first one - the adjustment period - lasts about one minute during which the subject approaches the steady level - which is typical for the second period.

Only the second period of about 4 minutes was used for calculations and only those curves where no clear trend towards improvement or deterioration

With the investigations by *Julesz* (1960 1963 1964) and others it has become clear that stereopsis cannot always be defined in terms of retinal disparity. According to *Lawson & Gulick* (1967) there are reasons to extend the concept of disparity to include not only the retinal disparities but also those induced on a higher visual level. In their experimental work, however, the same authors conclude that irrespectively of where the disparity is induced, stereopsis can be handled by the classical model of stereopsis.

For the purpose of this paper these questions concerning the physiological processes behind the nature of stereopsis are of secondary importance. If the patterns used as stimuli for the stereo perception are simplified, then it is the relative visual directions which are of importance for the information available to higher visual centers – a fact justifying the classical geometrical approach to stereopsis.

Using different test objects and experimental arrangements many investigators (for ref. see *Hirsch & Weymouth* 1948, *Foley-Fisher* 1968) have shown that the limiting values of the vernier and the stereo acuities are of about the same order of magnitude (about 2-10 sec. arc in the nodal point of the eye). It has also been shown that the two functions are equally influenced by changes in the luminance of the test object (*Leibowitz* 1955).

Although considerable information is available concerning vernier and stereo acuity as two separate visual functions, few systematic studies have been carried out on the relation between them.

The aim of this investigation has been to study the vernier and stereo functions from a quantitative point of view with a stimulus pattern which is supposed to give the same amount of information in the vernier and stereo situation respectively.

As *Ogle* (1962) emphasized it is essential in such a comparative study to use equivalent methods in testing the two functions.

The Stereo Vernier Situation

The main purpose in this investigation has been to obtain an experimental situation free from secondary cues which might influence the results, such as relative size of the targets, interposition, movement parallax or convergence.

As suggested by *Walls* (1943) a stereo vernier target (Fig. 1) is the adequate test object to use in an experimental investigation with the purpose of determining the relations between these two visual functions. Stimulated by the theoretical considerations of *Walls*, *Berry* (1948) took up the ideas of a stereo vernier test object. With a target consisting of two cylindrical rods, one above the other, he studied the vernier and stereo acuities under similar conditions. By changing the separation distance between the rods he was able to show that the two functions were not equally influenced by this procedure. Thus he found

can be identified. The criteria for excluding such curves have been a difference exceeding 5 steps between the first and last step of the second period.

The size of the easiest step (a_0) is so chosen that it is always correctly interpreted, whereas the smallest steps are so difficult that they are only guessed. To an object a_n we can adjoin a probability of correct interpretation, p_n , which goes from 1 to 0 with increasing difficulty (if allowance has been made for the chance of correct guessing). During the course of testing a number of transitions are made on a set of objects $\{a_n\}$ (Fig. 4). It is possible to estimate the probabilities connected with the objects from the numbers of these transitions.

The whole set of probabilities $\{p_n\}$ has not been determined at each testing period for practical reasons. It can be shown (Akai 1967a) that the probability of the step corresponding to the mode of distribution being perceived is ≥ 0.6 .

Since the distribution of transitions in the second period can be considered as symmetrical around a mean value it has been convenient to characterize the distribution by the arithmetic mean (M) and the standard deviation ($s.d.$). This mean value has arbitrarily been denoted "the threshold value".

In order to reduce the effect of temporary fluctuations of the level of performance each of the experimental sessions has been repeated on another independent occasion. The results presented in the following section are the averaged values.

Results

(a) Obtained with target Type A

The individual results are given in Table I for each of the five different separation distances between the reference lines and the dislocated part of the line.

The mean values of the five subjects are given as a graph (Fig. 5) where the ordinate indicates the threshold values and the abscissa the separation distances.

(b) Obtained with target Type B

The test object of Type B can be regarded as one of Type A with the separation distances $b = 0$. The results are presented as those for Type A (Table II and Fig. 6 respectively).

(c) Binocular vernier performance versus monocular performances

The results are presented in Table III and in a graph (Fig. 7). Target Type A with the same separation distances as earlier described has been used as test object.

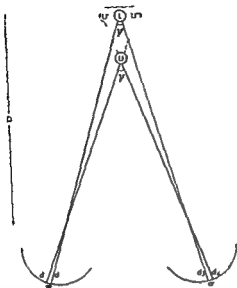


Fig 1

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$$\text{angle of disparity } (\eta) = \gamma - \gamma' = \frac{2a}{D}$$

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Method

With a new automatic technique described by Krakau (1967a) using a square wave on an oscilloscope as the same test object for both the vernier and the

Table I
Vernier and stereo thresholds related to the separation distance (Type A)

Extension of the target (min arc)	14		18		24		34		50	
b (min arc)	2		4		7		12		20	
Subject	ζ_1	η_1	ζ_1	η_1	ζ_1	η_1	ζ_1	η_1	ζ_1	η_1
G L	46	37.2	74	13.9	106	9.1	126	14.5	178	17.5
G S	49	23.0	50	10.1	72	7.5	113	14.5	151	18.7
V W	24	21.0	39	8.0	74	10.6	74	11.6	157	14.2
I B	46	16.9	77	6.5	124	7.5	118	10.6	162	16.3
O W	53	16.6	71	7.7	108	9.5	133	12.8	175	14.8
\bar{M} ($n=5$)	44	22.9	69	9.2	97	8.8	114	12.8	165	16.3
s.d.	11	8.4	17	2.9	23	1.5	23	1.7	12	1.9

The vernier (ζ) and stereo (η) thresholds are expressed in sec arc

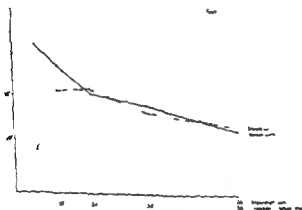


Fig 5
 Curves relating the thresholds (in sec arc) of the vernier and the stereo functions to the vertical separations (b) and the extension (c) target Type A. Average values for 5 individuals

(d) Precision of the results

An examination of the individual step curve will reveal fluctuations of the

stereo performances it has been possible to study the vernier and stereo acuities during identical situations and to make the comparison of the results on the bases of graphically recorded acuity determinations

(a) The Apparatus

A full description of the apparatus will be found elsewhere (Krakau 1967a) and only some of the arrangements which are essential or original for this investigation are mentioned here

A square wave on an oscilloscope screen is used as test object and is in itself an example of a vernier situation (Fig 2). It has two alternative positions in a random way and with equal chances the middle segment of the wave is displaced up or down

The size of the displacement of the middle segment can have a series of

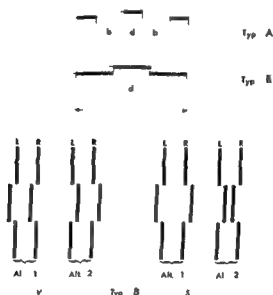


Fig 2

Two sets of test objects are used Type A and Type B each with the total extension (e) consisting of two reference lines (r) and a middle segment (d) which is displaced from the reference lines with a variable distance (a). In Type A r is kept constant (3.3 min arc) and a separation distance (b) has been varied (2, 4, 7, 12 and 20 min arc) giving the different values of e (14, 18, 24, 34 and 50 min arc). In Type B the same values of e have been used b = 0, r = d = 1/3 e. The two test objects on the top of the figure illustrate the targets as they are seen on the oscilloscope screen without the prismatic device. The four pairs of objects on the bottom of the figure illustrate the non fused images of a target Type B when it is observed with the prismatic device in vernier and stereo situation respectively.

Table II
Vernier and stereo thresholds related to the extension of the target (Type B)

Extension of the target (min arc)	14		18		24		34		50	
Subject	ζ	η	ζ	η	ζ	η	ζ	η	ζ	η
G L	30	48.9	36	48.0	30	28.5	34	21.4	44	24.0
G S	28	38.6	25	44.8	31	31.5	33	44.8	47	32.5
V W	29	56.1	20	61.8	27	39.3	24	43.2	30	49.8
I B	27	48.0	40	38.6	51	32.0	56	24.5	46	29.0
O W	30	35.1	27	34.4	41	66.6	64	37.2	43	23.0
M (n = 5)	29	45.3	30	45.5	37	39.6	42	34.2	42	31.7
s d	0.1	8.5	0.8	10.5	1.0	15.6	1.7	10.7	0.7	10.8

The symbols used are the same as those in Table I Thresholds in sec arc

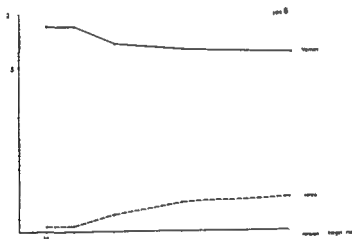


Fig 6

Curves relating the thresholds (in sec arc) of the vernier and the stereo functions to the extension (c) of target Type II Average values for 5 individuals

curve around a certain mean level. When calculated on step values the dispersion is of the same order of magnitude for all the observers. The standard deviation varies between 0.5 and 3.0 with an average of 1.520. The dispersion is about the same for all kind of targets and for both kinds of visual functions. Besides these fluctuations within one examination variations can also be

discrete values (steps) $\{a_0, a_1, \dots, a_n\}$ The ratio between two consecutive steps $\{a_n, a_{n-1}\}$ is 1/2

The subject has to interpret the position of the test object and when he presses one of two buttons in front of him (one for each position) his interpretation is transferred back to the apparatus. After three consecutive and correctly interpreted choices the dislocation $\{a\}$ is decreased one step (by a factor 1/1.2). If the observer cannot perceive a certain disparity – and does not press the button within a certain exposure time – or if the position of the disparity is not correctly interpreted the dislocation $\{a\}$ is increased one step (i.e. by a factor 1.2). The performance is automatically recorded and the step curve obtained denoting the sizes of the objects shown can be analyzed for instance in the way which will be described in a following section.

(b) The Test Objects

Two different sets of test objects have been used for the examinations of the stereo vernier relationship (Fig. 2). In type A there is a separation $\{b\}$ between the reference lines and the displaced middle segment. The separation $\{b\}$ has been varied and the thresholds of the vernier and stereo function have been determined for five different values of b : 2, 4, 12, 20 min arc. The two reference lines $\{r\}$ and the displaced part of the line $\{d\}$ were all of same length (9.3 min arc) and the total extension of the five modifications of Type A will thus be determined by the different separation distances used.

The test object of type B consists of a continuous broken line. The length of the displaced part is 1/3 of the total extension of the test object and the five different modifications used all have the same total extension as those of type A.

(c) The Prismatic Device

The binocular perceived vernier situation originated from a square wave can be perceived as a stereoscopic one – if certain conditions of the test object are fulfilled – by means of a prismatic device designed by Arakau (1961b) in front of the observer. It consists of two Dove prisms, one in front of each eye, without focal power and with the quality of rotating an image in the frontal plane without changing the direction of the light. When a Dove prism is rotated 90° about its horizontal axis the image is rotated 180°.

With this prismatic device the image of the horizontally extended square wave could easily be rotated clock wise or counter clock wise. In the stereo vernier experiments the vernier situation was always examined binocularly and with the lines of the test object in a vertical position (Fig. 2).

To produce a stereoscopic situation from a vernier situation one of the

Table III
Binocular and Monocular Vernier Thresholds

Extension of the target (min arc)	14		18		24		34		50			
	■		■		■		■		■			
b (min arc)	4		7		10		20					
Subject	Bin	1st eye	2nd eye	Bin	1st eye	2nd eye	Bin	1st eye	2nd eye	Bin	1st eye	2nd eye
C S	50	50	95	72	60	97	68	85	152	152	150	180
V W	43	38	47	38	86	88	68	87	105	112	92	177
L G	53	57	87	58	63	100	97	88	155	93	165	190
M	49	48	76	56	70	95	84	87	157	121	129	182
(n = 3) s.d.	0.6	1.0	0.66	1.7	1.4	0.6	1.5	0.2	2.8	2.8	3.7	0.7
										8.3	3.4	7.2

The eye with the best vernier performance monocularly is denoted as 1st eye Thresholds in sec arc

prisms was rotated 90° in order to present an image rotated 180° to one of the eyes (Fig 2 and 3) The displaced part of the square wave gives the transverse disparity necessary for the perception of stereopsis and the observer just has to determine whether the middle segment of the target ■ situated in front of the reference lines or behind them It must be observed that with this method of producing a stereo situation the pupillary distance is of no importance

The two disparate images so produced are easily fused by most observers with normal bifoveolar fixation The sum of the vernier off sets - the stereo disparity - must of course be within the limits of Panum's zone and the test object on the oscilloscope screen must be symmetric with regard to a vertical plane in the center of the target

By means of this prismatic device any type of heterophoria of the observer's

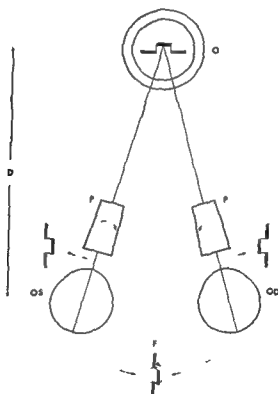


Fig 3

Schematic illustration of the method by which a stereoscopic situation is produced By means of a prismatic device (P) the images of the square wave on the oscilloscope (O) are rotated clock wise for the left eye and counter clock wise for the right eye When the images are fused a transverse disparity is produced The displaced segment of the target is perceived either in front of or behind the plane of the reference lines depending on the direction of the displacement (a)

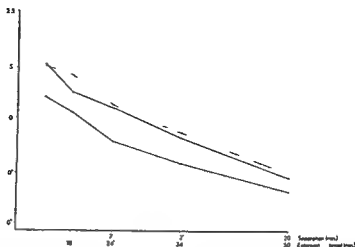


Fig 7

The relation between binocular (dotted line) and monocular (continuous lines) vernier performances. The upper continuous line represents the best monocular vernier performance (right or left eye) and the lower line the result obtained with the other eye. Target Type A with different separation distances (b) has been used. Average values for 5 individuals.

suspected from one day to another owing to varying degrees of attention. That is the reason why every subject has been re-examined on a later occasion. The differences between the results obtained in two identical examinations have been calculated. For the different types of targets they are (in steps): Vernier (A and B) = 0.0231 ($M = 1.2$), Stereo (A) 0.144 ($M = 2.0$) and Stereo (B) 0.269 ($M = 3.2$).

Discussion

(a) The Vernier Performances

The lowest threshold values of the vernier function for those trained subjects are obtained with the target Type B. The optimal intra-individual results vary between 2.0 sec arc and 3.0 sec arc (Table II). These values are in good agreement with the results previously reported (for a review see Foley, Fisher 1968) but a comparison with earlier results mostly obtained with a target of type "black on white" and with different statistical methods must be made with caution owing to the special kind of experimental technique used in this study.

Considering the results with target Type B (Fig. 6) however, it is apparent that in spite of the increasing length of the target there is no improvement of the vernier function. If the vernier offset is $1/3$ of the total length of the line, most observers achieve a better performance with a shorter type of test object.

eyes can be compensated. This can be accomplished by changing the position of the axes of the prisms. With two micrometer screws the prism axes are most carefully adjusted with regard to the optic axes of the eyes.

() Monocular and binocular vernier functions

From experiences with the stereo vernier situation it seemed logical to study also the monocular versus the binocular vernier function.

The examination of monocular and binocular vernier performances was carried out in principally the same way as previously described. In a random way the subject had to interpret a vernier pattern (target Type A) with its different separation distances monocularly or binocularly. In order not to produce a change of the size of the pupil in the monocular situation by occluding the contralateral eye a diffusing filter was placed in front of that eye. Three experienced subjects took part in the examination.

(e) Experimental arrangements

Throughout the various experiments all parts of the arrangement were kept constant. The illumination of the room (of about 15 lux) the luminance of the test object and the background illumination on the oscilloscope screen were chosen to give optimal viewing comfort and visual acuity. In some of the experiments a background target consisting of concentric circles was used as a stimulus for fusion. During the course of the experiments however it turned out to be unnecessary to use this fusion stimulating background since all the experiments were made in an orthophoric state of binocular vision. It was found that the reference lines (r) alone were a stimulus for fusion strong enough to maintain a stable bifoveolar vision throughout the examination session.

It is known from earlier experiments (Baker 1949, Foley, Fisher 1968) that vernier acuity is dependent on the wave length of illumination. In this investigation the background on the oscilloscope was pale yellowish green and the test object itself had a radiant energy distribution with its maximum in the middle of the visible spectrum (5100 Å).

The subject was placed 5 m in front of the test object viewing the target through the prismatic device. Uniformly illuminated unstructured screens with small apertures restricted the binocular field allowing nothing else but a field subtending 8° around the test object to be seen by the observer. Due to the rotating effect of the prisms it was necessary to have a neutral surrounding visual field.

Each experimental session consisted of a stereo vernier block of 10 min (Fig. 1) 5 min for each situation starting with one of the targets presented either in the vernier or stereo situation in a random way. The maximum expo

contrary to the earlier findings with targets of type two peg test (French 1920 Bar 1953 Ludvigh 1953) If a separation distance (b) is introduced between the test details as in target Type A a definite correlation is found between the magnitude of b and the corresponding thresholds of the vernier function (Fig 5) As can be expected the narrower the separation the lower are the thresholds obtained It is in accordance with the optimal level obtained with target Type II which can be considered as a borderline case of Type A where $b = 0$

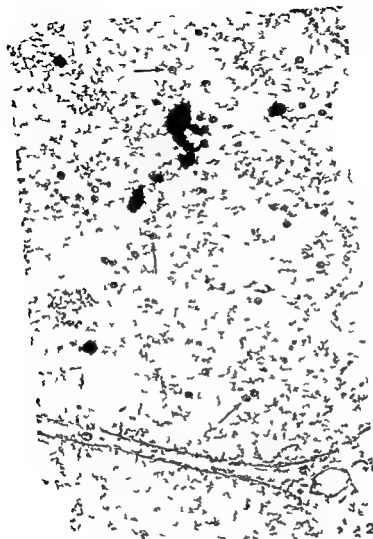
The impairment of the vernier function which was reported by some investigators (Berry 1948 Ludvigh 1953) when the reference lines (or dots) are brought close to the vernier off set - a fact difficult to explain - could not be demonstrated in the present material

(b) The stereo performance

It is apparent from Figs 5 and 6 that the lowest threshold values of the stereo function are obtained with a test object of Type A with the intrasubject variation between 6.5 sec arc and 9.1 sec arc The mean value for the five subjects (7.8 sec arc) is of the same order as that found with other methods (for references see Matsubayashi 1939 and Graham 1966) In earlier literature however there are no reports on stereo acuity with a test object of this vertically arranged three rod test. A somewhat lower threshold is found with the present method if the test used is arranged in accordance with Helmholtz three rod test. A test object of that kind has not been used in these experiments however because there is no vernier situation comparable to this target

There are some characteristic features of the stereo curves compared with the vernier ones. Contrary to the findings in the corresponding vernier situation there is an impairment of the stereo function if the angular separation (b) of the test object, Type A, is decreased from the range 4 / min arc to 2 min arc (Fig 5). This is consistent with the breakdown of stereo obtained with the test object Type B (Fig 6). Thus it can be concluded that a separation of a definite magnitude (4.7 min arc) is necessary to obtain an optimal stereo function if the present experimental method is used.

The deterioration of stereo acuity for targets with a narrow separation between the test details was also found by Berry (1948) who explained the stereo breakdown as probably attributable to the importance of ocular muscle balance in the depth situations. This conception of a deteriorating effect on stereo acuity due to a heterophoria or an induced phoria will also be found elsewhere in the literature on the subject (Litniskij 1939 Palmer 1962) but most authors conclude that there is no correlation between stereo acuity and the degree of the heterophoria under optimal viewing conditions (Nichols 1950 Sochsenweger 1956 Maki 1968).



Fig

Figure 1: A cell nucleus at a somewhat higher magnification. Intranuclearly located structures morphologically identical to herpes simplex virus are shown (arrows) $\times 20,600$

in thin sections cut through the center of the core (Fig 3 arrow). When the core was opaque throughout the reason was generally tangential sectioning. In most cases the core was located centrally within the capsid. A peripheral position could also be seen, however (Fig 5). The mean diameter of the core was 400 nm.

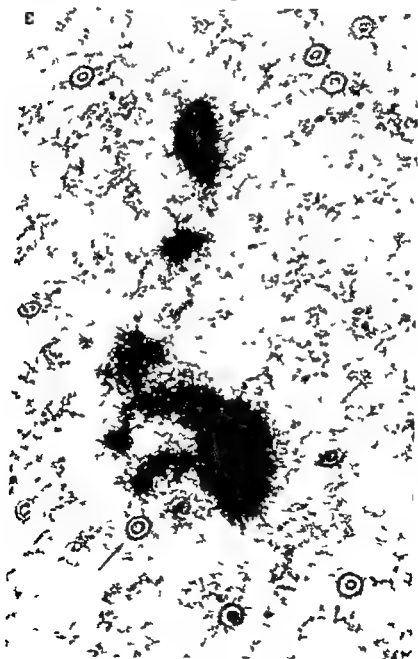
The capsid, which is a protein shell surrounding the core, was spherical or

slightly oval. Its mean diameter was 900-950 Å. In the sections it appeared as a dark ring surrounding the core. Most virus particles present in the cells of this clinically undamaged corneal

× 60 000

Enlargement of part of Fig 2. Each virus particle consists of an inner core and an outer capsid. A particle cut through the center of its core is indicated by an arrow.

Fig 3



As mentioned in a previous section any heterophoria in this investigation was compensated by the prismatic device and cannot interfere with the results. Some pilot studies on heterophoria and its relation to stereo acuity have been made with the same technique (Stigmar 1968 unpublished data). The stereo acuity was determined during 10 minute periods for different angles of induced heterophoria. But for extreme cases when the angle was at the limit of the fusional amplitude these experiments failed to show any correlation between the heterophoria and the stereoscopic acuity.

It can therefore be concluded that there is no support for the view that the stereo breakdown with narrower or no separations (b) is caused by an ocular imbalance. Another explanation must be discussed.

One essential factor may be the stereo deteriorating effect of contours described by Burian (1951). When fusion of disparate images gives rise to stereopsis there will be a shift from the primary subjective visual directions to a single visual direction. Burian states that the assimilation of visual directions as they occur in stereopsis is impossible if the corresponding centers are stimulated at the same time. The result of such stimulations is that fusion is partially lost and the character of the stereoscopic depth perception is changed. The stereoscopic vision in this situation corresponds to the range of patent stereopsis without fusion according to Ogle (1962) where the relationship between stereo acuity and disparity becomes less definitive.

Even if there is no distinct contour in a geometric sense in the area of the resulting new visual direction when targets Type A and II are used this area is stimulated by the diffraction and aberration discs induced by the illuminated test object. The luminance distribution must also induce some kind of lateral inhibition (v. Belesy 1968). In fact the closer the reference lines are situated the more these lines act as they would in a situation of two point resolution.

This geometric and schematic conception of stereoscopic vision seems to be in conflict with Julesz experiments (1963) with computer generated random stereo images. In these experiments it was shown that the same transverse disparity ("horizontal shift") was perceived with different qualities of stereopsis by changing the contours or even in the absence of distinct contours. As regards the stereo pairs used in these experiments devoid of familiar cues and without recognizable disparities in a geometric sense they will still give rise to retinal images with a light distribution on corresponding retinal meridians as if a real geometric disparity existed in the stereo pairs. Thus the prerequisite for stereopsis is given but the complex patterns of the objects make it difficult to analyze the various factors separately which in a secondary way might reduce the magnitude of depth perception.

With the present method of examining stereoscopic vision no secondary cues can influence the results. The pupillary distance of the subject is of no importance for the magnitude of the stereo disparity and the size differences of



A

the vessels are not brought out by the periodic acid Schiff technique because the vessels are covered with profuse chromatophores. The chromatophores contain a dark brown pigment melanin which is insoluble in water, alcohol, fat solvents and dilute acids and alkalis but soluble in strong alkalis and bleachable by powerful oxidising agents such as potassium permanganate (Ogilvie 1945, Lillie 1954).

Bleaching of melanin was used in the past to study the choroid vasculature after a Neoprene injection (Ashton 1953). Periodic acid Schiff staining without a preceding injection was applied in the present work. The vessels stain light

the retinal image which have been a source of error with many of the conventional stereo measuring methods (Graham 1966) are eliminated here

(c) The relationship between vernier and stereo functions

From the previous discussion it is evident that there exists a stereo deteriorating effect, which becomes more evident with decreasing separation distances while the vernier function gradually improves under the same conditions. Consequently the optimal values of the two functions cannot be the accurate basis for a comparison.

From Fig 5 and 6 it can be seen that the stereo performance – for any value of b – does not yield results better than those obtained in the vernier performance contrary to the findings of Berry (1948).

As is clearly demonstrated in Table I and in Fig 5 there is a close consistency between the threshold values of the vernier and stereo functions for corresponding values of b in the range of $b = 7-20$ min arc. In fact no significant difference can be shown between the threshold values for the two kinds of vision. The increased spreading of the stimulating pattern (following the increasing value of b) seems to affect the two visual functions equally. This close parallelism between the vernier and the stereo curves in the right part of Fig 5 makes it probable that the same measuring mechanism is involved and sets the limits of the quantitative capacity of the two visual functions which also has been suggested by Roelefs (1948). With this presumption further aspects on the relationship can be pointed out.

The probability of perceiving the vernier off set is the same as the probability of perceiving the total stereo disparity within the range of $b = 1-20$ min arc. But this stereo disparity is composed of two smaller vernier off sets each of them half of the total disparity. That means that a stereo disparity – at threshold – can be perceived although its constituent vernier parts cannot be perceived.

Consequently it can be stated that the thresholds of the vernier function are not limited by factors on the retinal level but by the capacity of higher visual centers because the retinal receptors have the capacity of detecting and codifying a vernier off set of half the magnitude of the smallest stereo disparity that can be perceived.

Now the question arises if a binocularly perceived vernier off set – at threshold – can also be considered as being composed of two subliminal monocular vernier off sets. From the results in Table III and Fig 7 it can be seen that there is no significant difference between the results obtained monocularly – if the performance with the eye with the best vernier acuity is considered – and the results obtained binocularly. The conclusion must be that there are no signs of an additive visual mechanism in the binocular vernier situation like that found in the comparable stereo situation.

This conclusion is in accordance with the presumption earlier made that the vernier and stereo acuities are both based on the perception of the relative visual directions and furthermore – no quantitative information is being lost in the visual process where the "half-images" of the two eyes are transformed into a three dimensional perception

Summary

The vernier and the stereo functions have been studied with a new automatic technique. The test objects have been produced on an oscilloscope screen and identical test objects have been used for testing both visual functions. The thresholds obtained are of the same magnitude as those obtained with methods previously used. The main results can be summarized as follows

1 The thresholds obtained vary considerably with the shape of the test object. Two different sets of test objects have been used, one of them consisting of a continuous broken line (Type B), one of them consisting of three vertically arranged lines where the middle non aligned line is separated from the two reference lines by a gap (Type A). Type B yields optimal vernier thresholds but increased stereo thresholds, contrary to the findings with the test object type A where a parallelism of the two visual functions can be demonstrated. When the separation distances between the test details are decreased in test object Type A which thus approaches Type B, a stereo deteriorating effect can be demonstrated. In order to secure a maximum stereoscopic efficiency the separation distances must be within a certain range.

2 The stereo vernier relationship has been studied. For the test object Type A the same limiting values for both functions can be demonstrated, suggesting that the thresholds for the perception of a stereo disparity and a vernier offset respectively are the same. A similar basic "measuring mechanism" may therefore be involved in stereoscopic vision and in the vernier situation.

3 Experiments with the monocular and binocular vernier function fail to show any clear difference between the thresholds obtained monocularly with the best eye and binocularly.

Acknowledgement

This work was supported in part by grant No. U 15/69 from the Delegation for Applied Medical Defence Research of the Swedish Ministry of Defence and by grants from the Medical Faculty of University of Lund.

vation of irideal vascular patterns and does not admit of any histological scrutiny of irideal vessels

The iris has sensory vasomotor and motor nerve fibres of which the last supplies the iris muscles. They are not visible by ordinary staining methods (Hogan & Zimmerman 1962). For examining the finer innervation of the rabbit's iris and the irideal vasculature the iris was sectioned into flat layers and the silver carbonate method was used on formalin fixed material and the osmium zinc iodide method on fresh material (Lassmann 1964). In this work the myelinated afferent nerves of the pig iris are visualised in flat preparations after potassium permanganate bleaching by the periodic acid Schiff technique. In frozen sections myelin of peripheral nerves stains a vivid red to red purple by the periodic acid Schiff procedure. This reaction was obtained in material fixed with formaldehyde and chromated before dehydration and embedding (Lillie 1954).

The flat preparation of the pig iris is fairly thick. Its thickness prevents more detailed study of the morphology of the vessels. The preparation is therefore thinned by means of trypsin digestion. This method will be described in a subsequent work.

Summary

The flat mount method for studying the vessels and the myelinated nerves of the pig iris is described. With this procedure the vessels and the myelinated nerves of the iris are demonstrated by periodic acid Schiff staining after potassium permanganate bleaching. The thickness of the preparation is a disadvantage of the method and trypsin digestion is therefore recommended.

References

- Ashton N. Central areolar choroidal sclerosis. A histopathological study. *Brit J Ophthalmol* 37: 140-147, 1953.
Ashton N. Vascular changes in diabetes with particular reference to retinal vessels. *Brit J Ophthalmol* 33: 407-420, 1949.
Friedenwald J. A new approach to some problems of retinal vascular disease. *Am J Ophthalmol* 32: 487-498, 1949.
Hogan M J & Zimmerman L E. *Ophthalmic pathology. An atlas and textbook*. Ed 2. Saunders, Philadelphia & London, 1962.
Lassmann G. Zum problem der Nerven- und Gefassversorgung der iris des kaninchens. *Ophthalmologica* 147: 467-484, 1964.

References

- 1 *Bair H* See discussion in the paper by Ludvigh E 1953
- 2 *Baker A E* Some variables influencing vernier acuity *J Opt Soc Amer* 39 56, 56 1949
- 3 *v Békésy G* Mach and hering type of lateral inhibition in vision *Vision Res* 8 1483 1499 1968
- 4 *Berry R V.* Quantitative relations among vernier real depth and stereoscopic depth acuities *J Exp Psychol* 34 103 121 1948
- 5 *Burton H.* Stereopsis *Docum. Ophthal* 6 160 183 1951
- 6 *Colenbrander M C* De grenzen van het stereoscopisch zien *Ned Tijdschr Geneesk*, 90 809 812 1948
- 7 *Foley Fisher J A* Measurements of vernier acuity in white and coloured light, *Vision Res* 8 1055 1065 1968
- 8 *French J W* The unaided eye Part III *Trans Opt. Soc London* 21 127 156 1920
- 9 *Graham C H* Visual space perception in vision and visual perception (Edited by Graham, C H Wiley & Sons Inc New York) 1966
- 10 *Hirsch M J & Weymouth F W* Distance discrimination *Arch Ophthal* 39 221 231 1948
- 11 *Jules B* Binocular depth perception of computer generated patterns *Bell Syst. Tech J* 39 1123 1161 1960
- 12 *Jules B* Stereopsis and binocular rivalry of contours *J Opt Soc Amer* 53 994 999 1963
- 13 *Jules B* Binocular depth perception without familiarity cues *Science* 145 356 62 1964
- 14 *Krakau C E T* An automatic apparatus for time series analysis of visual acuity *Vision Res* 7 99 105 1967a
- 15 *Krakau C E T* En metod for fortlopande provning av stereosynskarpan *Tidn Forsvarsmedicin Stockholm* 14 (In Swedish with abstract in English) 1967b
- 16 *Lawson R B & Gulich W L* Stereopsis and anomalous contour *Vision Res* 7 271 297 1967
- 17 *Le Grand Y* *Optique physiologique* (Editions de la Revue d'optique Paris) 3 224 227 1956
- 18 *Leibowitz A* Some factors influencing the variability of vernier adjustments *Amer J Psychol* 68 266 273 1955
- 19 *Links A* *Vision in Physiology of the eye* (Grune and Stratton, New York) 9 507 533 1952
- 20 *Lisitskiy G* *Soviet Vestn Oftalm* 69 661 1939 (Cited by Sachsenweger 1956)
- 21 *Ludvigh E* Direction sense of the eye *Amer J Ophthal* 46 139 143 1953
- 22 *Maki O* Studies on deep sensation, *Acta Soc Ophthal Jap* 1968
- 23 *Matrubayash A* *Forschung uber die Tiefenwahrnehmung* *Ber Ges Physiol* 110 464 466 1959
- 24 *Nichols H* *Amer J* 33 1591 1950
- 25 *Ogle A V* Disparity limits of stereopsis *Arch Ophthal* 48 50 60 1952
- 26 *Ogle A V* *Theory of stereoscopic vision* In *psychology A study of a Science* 1 (Edited by S Koch Mc Graw Hill New York) 1959
- 27 *Ogle A V* Spatial localization through binocular vision In *The Eye* 4 (Edited by Davson H Academic Press London) 1962

chamber angle changes in eyes with retinal detachment compared to the fellow eyes the following study was performed

Material

Material 1

Age and sex distribution The total number of patients with retinal detachment hospitalized in our department in the two year period 1967-1968 were 267 (128 males 139 females) with an average age of 51.8 years for males and 58.4 years for females. This difference in average age is significant (Student's *t* test $t = 3.166$ $P < 0.01$). There is also a slight female prevalence (52.1%) but this is not significantly different from the norwegian census population (females 50.2%).

The ratio of females to males in the different age groups is however not constant neither in the detachment material nor in the census population (Statistical Yearbook 1968). This variation in ratio is visualized in fig 1. Among the detachment patients there is a male prevalence in the lower age groups and a female prevalence in the higher age groups. When compared with the census population it is however only the male prevalence in the age groups from 30

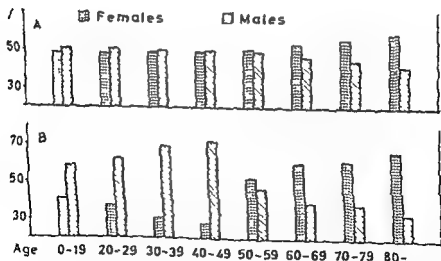


Fig 1

A Ratio of females to males in census population in the different age groups. Total number = 9.8×10^6 . B Ratio of females to males in the age groups of retinal detachment material 1. Total number = 267.

- 28 *Palmer D A* Binocular eye movements and stereoscopic depth discrimination *Opt Acta* 9 311 334 1962
- 29 *Roclofs C O* See discussion in the paper by Colenbrander (1948)
- 30 *Sachsenweger R* Der Einfluss von Heterophorien auf das raumliche Sehen *Dtsch Gesundh Wes* 11 883 890 1956
- 31 *Walls G L* Factors in human visual resolution *J Opt Soc Amer* 33 487 505 1943

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TRAUMA AND RETINAL DETACHMENT

The anterior chamber angle with special reference to width,
pigmentation and traumatic ruptures

BY

PER SYRDALEN

Traumatic ruptures in the anterior chamber angle are frequently seen as a result of ocular contusion (Tonjum 1966). When these changes are seen in eyes with retinal detachment they may be taken as proof of previous ocular contusion (Wolff & Zimmerman 1962, Cox *et al* 1966). A history of trauma is very often reported by retinal detachment patients and it would be of interest to know the incidence of chamber angle ruptures due to contusion in these eyes.

Gonoscopic findings in eyes with retinal detachment have been reported by Sebestyen *et al* (1962) but chamber angle lesions due to contusion were not dealt with by these authors and the incidence of these changes in eyes with retinal detachment has not yet been evaluated.

Pigmentation of the anterior chamber angle occurs more frequently with advancing age both in normal and in glaucomatous eyes (Zuege *et al* 1961) and more frequently in glaucoma capsulare than in eyes with primary open angle glaucoma (Horven 1966). As retinal detachment is a disease of age and also a disease seen in connection with trauma, eye surgery, uveitis and other eye diseases, angle pigmentation is not expected to be less in detachment eyes than what seen in a normal population.

In order to get more information about width, pigmentation and traumatic

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FLAT PREPARATION METHOD FOR STUDYING BLOOD VESSELS AND MYELINATED NERVES OF THE PIG IRIS

BY

MATTI SAARI

Because of the laminar structure of the eye flat preparations afford an unusually favourable opportunity to study such structures as retinal and choroidal vessels corneal and trabecular endothelium lens epithelium and retinal pigment epithelium. The periodic acid Schiff technique has been used earlier for flat mount staining of the retina (Friedenwald 1949 Ashton 1949). Alone periodic acid Schiff staining is incapable of demonstrating the iris vessels and the myelinated nerves in flat preparations as the iris is rather thick and contains profuse melanin in chromatophores and in the pigment epithelium. However melanin of the choroid can be bleached with heavily oxidising potassium permanganate (Ashton 1953). A method based on these procedures for the demonstration of the vessels and the myelinated nerves of the pig iris by the flat mount technique is described in this paper.

Material and Methods

Pig eyes from an abattoir were used in the study. After enucleation the eyes were fixed in 10 per cent neutral formalin for a minimum of 24 hours. The eyes were opened equatorially. The vitreous and the lens were removed with

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Table 1
Norweg an census population (total 3 766 000) in d fferent age groups Ratio females/males in census population among retinal detachment patients (material I = 267 and material II = 227 patients) and among traumatic cases from material II (36 patients) N = number of patients (n) = number of patients each age group

Age groups (years)	0-19	20-29	30-39	40-49	50-59	60-69	70-79	80-
Census population $\times 10^{-4}$	1.35	499	409	505	461	363	216	78
Norway 1966								
Ratio females/males	0.919	0.953	0.972	0.994	1.025	1.159	1.210	1.400
Ratio females/males	0.700	0.600	0.444	0.359	1.115	1.326	1.000	2.000
Material I	(17)	(16)	(19)	(25)	(55)	(96)	(39)	(6)
N = 267 (n)								
Inhabitants per one detachment per year	79.91 ^a	34.316	34.08	40.220	9220	4160	6092	14.500
Ratio females/males	0.400	1.000	0.667	0.479	1.000	1.486	2.000	4.000
Material II	(14)	(12)	(10)	(20)	(46)	(87)	(35)	(5)
N = 227 (n)								
Ratio females/males	0.000	0.500	1.000	0.333	0.600	0.286	0.000	0.000
Traumatic cases	(5)	(3)	(4)	(4)	(8)	(9)	(2)	(1)
N = 36 (n)								

forceps and scissors. The iris, ciliary body and anterior choroid were freed in toto. The residue of the vitreous and the pigmentary layer of the iris were wiped off carefully with pieces of blotting paper. The ciliary process was cut away with small scissors as completely as possible (Fig 1). It was washed overnight in several changes of distilled water. It was then kept in 0.25 per cent potassium permanganate solution for four hours and washed in water kept in 5 per cent oxalic acid solution for six min and washed in running water for 10 min and finally washed in distilled water. The preparation was floated on a slide, dried and stained with PAS hematoxylin. For control purposes a part of the irises were halved: one half was stained without bleaching with PAS hematoxylin and the other half was stained after bleaching with PAS hematoxylin.

Results

The blood vessels and myelinated nerves were covered with profuse chromatophores in an unbleached iris and hardly any details of the vessels and nerves could be demonstrated (Fig 2).

In a bleached iris chromatophores were not seen. The vessels of the iris were visible. The major arterial circle of the iris and the radial vessels stained purple. Capillaries were not visualised however (Fig 3). The myelinated afferent nerves were clearly brought out by the periodic acid Schiff technique.

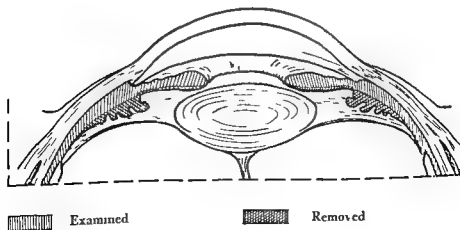


Fig 1

A drawing of the anterior part of the eye showing the anterior uvea used in the study and the ciliary process to be removed

to 49 years which may be considered statistically significant (30-39 years $\chi^2 = 6.448$ $P < 0.05$ 40-49 years $\chi^2 = 9.101$ $P < 0.01$)

In table I is listed the ratio of females to males in the age groups in the census population in retinal detachment material (I) and the estimated ratio of inhabitants to one detachment per year. This estimate is based on the assumption that our department treat roughly 55% of all patients hospitalized with retinal detachment in Norway. In the age group 0-19 years there is one detachment per about 80 000 inhabitants per year. The incidence then gradually increases up to the age group 60-69 years where there is one detachment per about 4000 inhabitants per year. Over 70 years the incidence seems to decrease a little. This decrease of incidence may well be artificial. The patients are old, some of them will not be seen by a doctor and some will not be hospitalized due to their high age.

Material II

A personal examination of all patients by the author was necessary to obtain uniformity in the criteria used to classify trauma, angle width, chamber angle pigmentation and traumatic chamber angle ruptures. Due to vacations, however, this could be performed only in 85% (227 patients = material II) of the total number of retinal detachment patients (material I) hospitalized in our department in the two year period.

There is no major difference in age and sex distribution between material I and material II. In material II 106 patients (46.7%) were males with an average age of 52.2 years and 121 patients (53.3%) were females with an average age of 59.3 years. The ratio of females to males in the age groups in material II is listed in table I and the sex distribution in the different age groups in material I and material II are illustrated in fig. 2.

The following presentation of the material refers to material II.

Both sexes show an insignificant prevalence to left eye (table II) detachment (53.7%). Redetachment in previously operated eye is seen in 2.2% and bilateral detachment in 7.5% of the cases.

Trauma. The different forms are listed in table III. The numbers in the table are mainly based on the predetachment case history given to the author from each patient. All patients were inquired for ocular trauma, blows to the head or accidents prior to detachment. The age distribution is seen in fig. 2 (C). There is no significant difference in average age between females (47.4) and males (45.6 years) in this group. There is, however, a highly significant difference ($\chi^2 = 12.45$ $P < 0.001$) in the ratio of males to females of the traumatic compared with the nontraumatic cases. The traumatic cases thus yielding a large prevalence of males.

1. *Perforating injury.* Four of these eyes had suffered severe (++) (table IX)

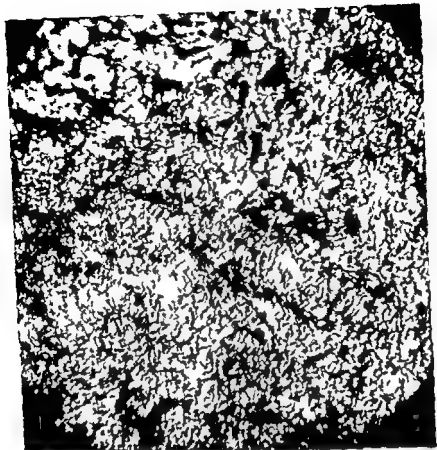


Fig 2

Flat preparation Unbleached iris of the pig Chromatophores obscure the vessels and the myelinated nerves PAS hematoxylin $\times 100$

in a bleached pig iris The myelinated nerves stained dark red purple There was a rich plexus of myelinated nerves in the bleached iris of the pig (Fig 3)

The flat preparation of the pig iris was however fairly thick and often worked loose on staining Its thickness prevented a more detailed study of the morphology of the vessels

Discussion

The retinal vessels have earlier been studied in flat preparations by the periodic acid Schiff technique (Friedenwald 1949 Ashton 1949) In an unbleached iris

Table III

Material II Trauma in predetachment history N = 36 (males = 27 females = 9)
One male is listed both as perforating injury (3½ years before detachment) and ocular
contusion (13 days before detachment) Both trauma were severe but the contusion
precipitated the detachment.

	Males	Females	Total
Previous perforating injury	5 (47%)	0	5 (22%)
Ocular contusion	18 (17%)	5 (41%)	23 (101%)
Indirect trauma	5 (47%)	4 (33%)	9 (4%)
No trauma in history	9 (45%)	112 (976%)	191 (841%)

with secondary endophthalmitis. In this eye vitreous changes and retinal degeneration were found upon admission but no other sign of previous perforating injury could be seen. Due to the severeness of the symptoms after a perforating injury it is not likely that cases belonging to this group have been overlooked.

2 Ocular contusion has been classified into three degrees of severity + (minor ocular contusions or contusions where little information about degree is available) ++ (more severe contusions where the patients have given detailed information about the accident) and +++ (severe contusions with hyphaema intravitreal bleeding or other obvious signs of contusion).

In the ocular contusion group are listed patients previously hospitalized due to ocular contusion (++ 1 +++ 5) seen by ophthalmologist because of ocular contusion but not being hospitalized (+ 1 ++ 1 +++ 1) giving a history of ocular contusion immediately followed by visual disturbances (+ 1 ++ 3 +++ 1) and patients reporting ocular contusion not seen by ophthalmologist and not giving visual disturbances or discomfort afterwards (+ 3 ++ 1).

17% of the males and 41% of the females gave a history of ocular contusion prior to detachment. (Minor injuries such as lesions in the conjunctiva corneal abrasions or anamnestic negligible ocular contusions without any symptoms afterwards are not listed as trauma in the table).

3 Indirect trauma. In this group are listed patients giving a history of blows to the head (5) or eye surroundings (4) followed by visual disturbances. The time interval between the indirect trauma and the beginning of symptoms has been from immediately after the trauma and up to 3½ months.

The time interval between the actual trauma and the occurrence of detachment is listed in table IV.

Some possible complicating factors seen in material II in detachment eyes



A

the vessels are not brought out by the periodic acid Schiff technique because the vessels are covered with profuse chromatophores. The chromatophores contain a dark brown pigment melanin which is insoluble in water, alcohol, fat solvents and dilute acids and alkalis but soluble in strong alkalis and bleachable by powerful oxidising agents such as potassium permanganate (Ogilvie 1945, Lillie 1954).

Bleaching of melanin was used in the past to study the choroid vasculature after a Neoprene injection (Ashton 1953). Periodic acid Schiff staining without a preceding injection was applied in the present work. The vessels stain light

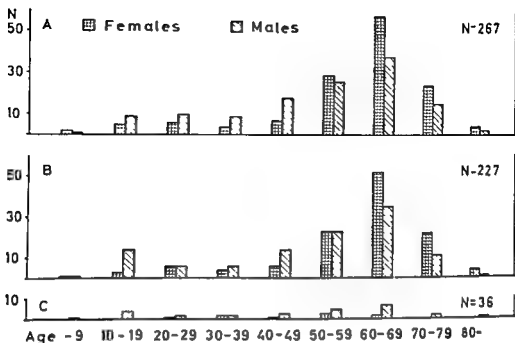


Fig 2

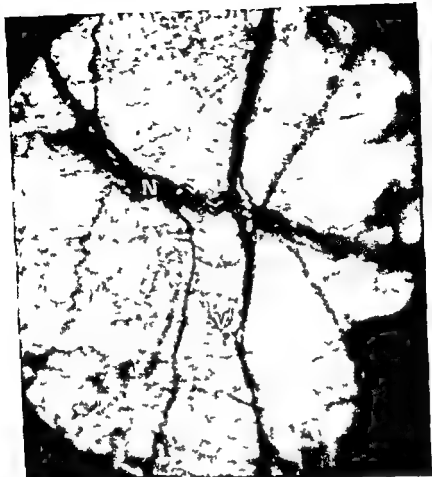
Age and sex distribution A material I (N = 267) B material II (N = 227) and C patients with trauma in predetachment history from material II (N = 36)

Table II

Material II Distribution right/left eye detachment Redetachment in previously operated detachment eye Previously operated detachment in fellow eye Bilateral detachment upon admission and total number of bilateral detachments N = 227 (males = 106 females = 121)

	Males	Females	Total
Detachment right eye	50 (47.2%)	59 (48.8%)	109 (48.0%)
Detachment left eye	59 (55.7%)	63 (52.1%)	122 (53.7%)
Redetachment	2 (1.9%)	3 (2.5%)	5 (2.2%)
Prev operat detach fell eye (a)	8 (7.5%)	5 (4.1%)	13 (5.7%)
Bilateral detach upon admission	3 (2.8%)	1 (0.8%)	4 (1.8%)
(b)			
Total number of bilat detach (a + b)	11 (10.4%)	6 (5.0%)	17 (7.5%)

perforating injuries due to metallic intraocular foreign body (2) and rupture of the bulb after blunt trauma (2) The fifth eye had a needle perforation (+)



B

Fig 3A and B

Fig 3A Flat preparation. A bleached iris of the pig. The vasculature and the myelinated nerves of the iris are visualised by the periodic acid Schiff technique. The major arterial circle of the iris (MC) and the radial vessels (V) have stained purple. The long posterior ciliary nerve (CN) and the myelinated nerves of the iris (N) have stained dark red purple. PAS hematoxylin $\times 40$.

Fig 3B The same preparation as in Fig 3A. Chromatophores are not seen as in Fig 2. The radial vessels (V) and the myelinated nerves (N) are visualised. PAS hematoxylin $\times 100$.

purple in bleached irises. But the capillaries are not visualised. This method makes it possible to observe histologically complete irideal vessels which can not be seen in serial sections of the iris. But this method prevents clear obser-

to know the incidence of pseudoexfoliation among patients suffering from retinal detachment in order to evaluate if any difference exists between detachment eyes and fellow eyes

In table VI are listed the results of a chi square test on the factors mentioned above of possible importance for the development or precipitation of retinal detachment. Of these only aphakia and angle ruptures are seen to be of importance

Material III

Selected material From material II all eyes harbouring eye diseases or possible complicating factors other than the actual detachment i.e. trauma, previous eye surgery, glaucoma, uveitis and pseudoexfoliation are excluded. Material III thus includes only patients with primary untreated uncomplicated retinal detachment in one eye and the other eye is apparently healthy. This selection has been done in order to evaluate the possible influence on chamber angle pig

Table VI

Material II Number of detachment eyes and fellow eyes with a history of uveitis, presence of aphakia and pseudoexfoliation, previously diagnosed glaucoma and presence of traumatic chamber angle ruptures. Results of chi square on the incidence in detachment eyes and fellow eyes

	Detachment eyes	Fellow eyes	Chi square	Significance level
Uveitis +	15	13	0.038	-
Uveitis -	212	214		
Aphakia +	27	9	8.719	$P < 0.01$
Aphakia -	200	214		
Pseudoex +	7	9	0.062	-
Pseudoex -	220	218		
Glaucoma +	8	7	0.000	-
Glaucoma -	219	210		
Angle rupt. +	13	0	10.644	$P < 0.01$
Angle rupt. -	210	209		

epithelium were found within the nuclei. The cytoplasm of these cells contained very few structures that could be identified as virus particles. The picture of the cells lining the air sac was quite different. A very large number of

Part of the cytoplasm (upper left corner) and part of the nucleus of another cell in the epithelium. Many intranuclearly located virus particles are seen. $\times 93,500$

Fig. 4



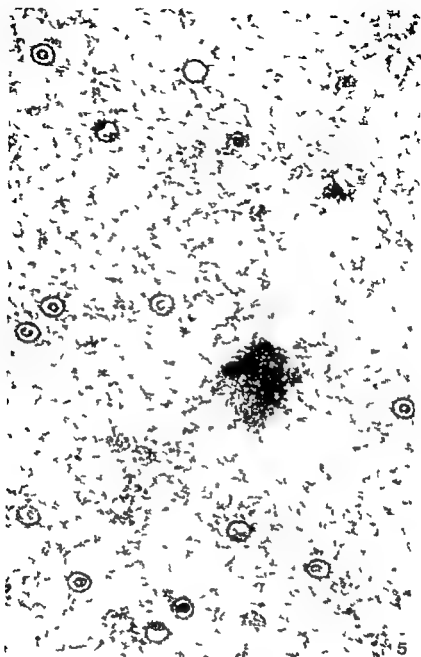


Fig 5

Enlargement of part of Fig 4 The material of the core is sometimes seen to be excentrically located $\times 58\,000$

virus particles were generally seen both in the cytoplasm and in the nucleoplasm

Extracellularly located virus particles in most cases surrounded by an additional envelope derived from cellular membranes were frequently seen in re

Table IV

Time interval between actual trauma and retinal detachment N = 36 (males = 9, females = 9) One patient is listed as (+ 1) in the perforating injury group (over 6 months) but the actual trauma was ocular contusion (0-4 weeks) See text table III

	Perforating injury	Ocular contusion	Indirect trauma
0-4 weeks	1	10	1
4-12 weeks	0	2	0
12 weeks-6 months	1	4	2
Over 6 months	2 (+ 1)	7	0

Table V

Material II Possible complicating factors in detachment eyes and fellow eyes N = 227 (males = 106 females = 121) One male fellow eye had been enucleated (tumor) but had previously been otherwise healthy (percentages calculated in relation to N = 106 in fellow eye group too)

	Detachment eyes			Fellow eyes		
	Males	Females	Total	Males	Females	Total
Uveitis in hist	8 (7.6%)	7 (5.8%)	15 (6.6%)	7 (6.6%)	6 (5.0%)	13 (5.7%)
Aphakia	14 (13.2%)	13 (10.7%)	27 (11.9%)	5 (4.7%)	4 (3.3%)	9 (4.0%)
Pseudoexfoliation	3 (2.8%)	4 (3.3%)	7 (3.1%)	4 (3.3%)	5 (4.1%)	9 (4.0%)
Glaucoma Prim + sec	5 (4.7%)	3 (2.5%)	8 (3.5%)	3 (2.8%)	4 (3.3%)	7 (3.1%)

and fellow eyes are listed in table V Included are a history of uveitis (6.6% 5.7%) aphakia (11.9% 4.0%) pseudoexfoliation of the lens capsule (3.1% 4.0%) and glaucoma (3.5% 3.1%) (previously diagnosed and under treatment)

Pseudoexfoliation is as retinal detachment a disorder of age A relationship between the two disorders is not known It would therefore be of some interest

- 5 Gonioscopy is of importance to prove the existence of previous ocular contusion
- 6 Traumatic retinal detachment (all forms) usually occurs in predisposed patients judged in relation to the condition of the fellow eye

Summary

A two year retinal detachment material of 227 cases is presented. The role of aphakia, glaucoma, uveitis and pseudoexfoliation is evaluated. Gonioscopic findings concerning chamber angle width, pigmentation and traumatic angle lesions are studied. 55.6% of the male and 60% of the female patients reporting ocular contusion had chamber angle lesions. The role of trauma and predisposing factors to retinal detachment is discussed.

References

- Aasved H. The geographical distribution of fibrilloglione epitheliocapsularis. *Acta Ophthalmol (Kbh)* 47: 810-812 1969
- Braathén H. Års amotiomateriale fra øyevædelingen Haukeland sykehus. Annual meeting Norsk Øyefagforening, June 1968
- Busacca A. La physiologie du muscle ciliaire étudiée par la gonioscopie. *Ann. Oculist. (Paris)* 188: 1-19 1905
- Bohringer H. R. Statistisches zu Häufigkeit und Risiko der Netzhautablösung. *Ophthalmologica* 131: 331-334 1950
- Cibis P. A. Vitreoretinal pathology and surgery in retinal detachment. The C. V. Mosby Company, Saint Louis, pp. 44-45 1965
- Cox M. S., Schepens C. L. & Freeman H. M. Retinal detachment due to ocular contusion. *Arch. Ophthalmol.* 76: 678-685 1966
- Duke Elder S. System of Ophthalmology. Henry Kimpton, London, Vol. VI, p. 394 1969
- Edmund J. The clinical picture and prognosis of retinal detachment. *Acta Ophthalmol (Kbh)* 42: 980-1014 1964
- Gruber E. Retinal detachment and its relationship to trauma. *Am. J. Ophthalmol.* 56: 911-919 1963
- Horten I. Exfoliation syndrome. *Arch. Ophthalmol.* 76: 505-511 1966
- Norton E. W. D. Retinal detachment in aphakia. *Am. J. Ophthalmol.* 58: 11-124 1964
- Scheie H. G. Width and pigmentation of the angle of the anterior chamber. *A. M. A. Arch. Ophthalmol.* 58: 510-512 1957
- Schepens C. L. & Marden D. Data on the natural history of retinal detachment. *Arch. Ophthalmol.* 66: 631-642 1961
- Schepens C. L. & Marden D. Data on the natural history of retinal detachment. *Am. J. Ophthalmol.* 61: 213-226 1966

Table III

Material II The inter ocellar angle WdF pigment and the angle between the eyes in C. nio copy in 2-3 d tachment eyes (males = 10 females = 118) and 90 d cell w eyes (males = 97 females = 11)

	Detachment eyes			Fellow eyes		
	Males	Females	Total	Males	Females	Total
C grade 0 (clear)	1 (1%)	1 (0.5%)	2 (0.5%)			
Open Gr I II		1 (0.9%)	1 (0.5%)	2 (1.8%)	2 (1%)	
Open Cr III IV	104 (99%)	117 (89.1%)	221 (99%)	97 (100%)	110 (98.7%)	207 (99.7%)
None/little pigment	72 (60.2%)	86 (70.9%)	158 (71.2%)	75 (75.3%)	92 (82.1%)	165 (79%)
Moderate pigm	14 (13.5%)	3 (19.5%)	17 (16.7%)	10 (10.3%)	15 (13.4%)	25 (11.7%)
Heavy pigm	18 (17.3%)	9 (7.6%)	27 (12.1%)	14 (14.4%)	5 (4.5%)	19 (9%)
Angle lesion	10 (9.5%)	3 (2.5%)	13 (5.8%)			

were confirmed by Regan & Rousseau (1966) and they concluded that "retinal detachment may occur in eyes in which the rate of aqueous flow and also the facility of outflow are primarily abnormal and that the detachment is not necessarily the cause of the altered hydrodynamics". An imbalance was suggested in the physiology of aqueous production and the normal mechanisms of outflow and absorption and this imbalance was found to be bilateral in some cases even if the detachment occurred only in one eye.

Our present knowledge indicate therefore that the hypotony frequently seen in eyes with retinal detachment is caused by a decreased formation of aqueous humor even sometimes also associated with decreased facility of outflow (Dobbie 1963, Becker 1963, Regan & Rousseau 1966).

Normally there is little difference in intraocular pressure between two healthy eyes of an individual (Davanger 1965). Individuals with an untreated retinal detachment in one eye and an apparently healthy other eye give excellent opportunity to use the other eye as control.

The aim of the present investigation is to study intraocular pressure in retinal detachment eyes to evaluate possible relationship between intraocular pressure and area of detachment, duration of detachment and number of retinal holes. Of interest is also the pre-operative ocular rigidity and the difference in intraocular pressure obtained by use of Schiotz tonometer and Goldmann applanation tonometer.

Material

The present investigation is performed on two groups of patients.

Group A This group consists of 124 patients (46 males and 78 females) with an average age of 57.6 years (10-81). There is no significant difference in average age for females (58.9 years) and males (55.4 years).

21 (45.7%) of the male and 28 (33.9%) of the female patients were classified as myopic (i.e. refraction minus 0.5 or more) and among these 7 males and 6 females had myopia minus 8 or more.

Group B This group consists of 37 patients (16 males and 21 females) with an average age of 57.3 years (17-79). As judged by the result of the Student's *t*-test ($t = 1.996$, $0.05 < t < 0.10$) there is no significant difference in average age for females (61.6 years) and males (51.8 years).

7 of the males (43.8%) and 2 of the females (9.5%) were myopic and of these 3 males and 1 female exceeded minus 8.

Group A patients were hospitalized during 1964-1968 and group B patients during 1969. All patients included in this investigation had primary retinal detachment (unoperated) in one eye and the other eye was apparently healthy.

mentation of the above mentioned factors. Material III includes 134 patients (51 males and 83 females)

Methods

All detachment eyes and fellow eyes (material II and III) were examined under the same conditions. Gonioscopy was performed with mydriasis obtained by topical use of Cyclogyl 1% (Cyclopentolate hydrochloride) and metaoxedrin chloride 10%. A Goldmann three mirror contact lens and a Haag Streit 900 slit lamp were used throughout.

The width of the filtration angle was classified from Grade IV (wide open) to Grade 0 (closed) as described by Sebestyen *et al* (1962). Grade IV means an angle in which the ciliary body band is visible throughout the whole circumference. Grade III means that the ciliary body band is invisible but the scleral spur is visible. In Grade II the scleral spur is invisible but the posterior part of the trabeculum is visible. In Grade I only part of the anterior trabeculum is visible and Grade 0 means an angle closed up to Schwalbe's line. Grade IV III corresponds to Scheie's (1957) Grade 0 wide open - Grade II narrow.

The pigmentation in the chamber angle was classified in three groups

1 *None/little pigmentation* which corresponds to Scheie's (1957) none pigmentation. 2 *Moderate pigmentation* which corresponds to Grade I II pigmentation by Scheie and 3 *Heavy pigmentation* which corresponds to Scheie's Grade III IV. This classification was thought to be sufficiently accurate due to the fact that all eyes both detachment and fellow were examined by the author and the same criteria used each time.

Traumatic chamber angle ruptures were classified after criteria given by Wolff & Zimmerman (1962) and Tonjum (1966). Tears of the anterior face of the ciliary body or iris root were taken as proof of previous ocular confusion. These changes may be difficult to discover if a long time has passed since the trauma. In this material the fellow eye served as control in the majority of patients. Only eyes in which the traumatic changes were clearly seen (and the other eye had no such changes) were listed in the traumatic angle lesion group.

Pseudoexfoliation of the lens capsule was determined under full mydriasis and the use of slit lamp.

Results

Material II. Table VII shows the results concerning chamber angle width pigmentation and traumatic chamber angle ruptures. Gonioscopy was performed

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INTRAOCULAR PRESSURE AND OCULAR RIGIDITY IN PATIENTS WITH RETINAL DETACHMENT

I Preoperative study

BY

PER SYRDALEN

Retinal detachment is usually accompanied by hypotony Kleiner (1933) reviewed the literature and reported results of own investigation. He stated that 75% of all detachment eyes had intraocular pressure lower than the healthy other eye. The hypotony increased with increasing time since the detachment occurred, increased with increasing area of detachment and was more pronounced in eyes with numerous and great ruptures in the retina. Acute and very extreme hypotony may accompany retinal detachment (Beigelman 1929) but a more moderate hypotony is the rule. Some detachment eyes will have raised intraocular pressure and even if the association of open angle glaucoma and retinal detachment is unusual (Becker 1963) it has been reported (Laaton Smith 1963, Sarin *et al* 1963, Guillaumat & Bonnin 1967).

The cause to the hypotony has not been explained by any change in ocular rigidity in detachment eyes (Ytteborg 1961, Rousseau & Regan 1965, Regan & Rousseau 1966) neither has the existence of an extraordinary outflow channel through the retinal detachment or retinal breaks been proved (Dobbie 1963, Regan & Rousseau 1966).

By using fluorescein technique and suction cup Dobbie (1963) found evidence of decreased formation of aqueous humor in detachment eyes. These results

Table V III

Material III The anterior chamber angle Width and pigmentation in selected part of material II N = 134 (males = 51 females = 83)

	Detachment eyes			Yellow eyes		
	Males	Females	Total	Males	Females	Total
O ₁ en Gr I II						
				1	1	2
				(12%)		(07%)
O ₁ en Gr III IV	51 (100 %)	83 (100 %)	134 (100 %)	51 (100 %)	82 (93.8 %)	133 (99.8 %)
None/little pigm	40 (78.4 %)	66 (79.5 %)	106 (79.1 %)	39 (76.5 %)	69 (83.1 %)	108 (80.6 %)
Moderate pigm	5 (9.8 %)	14 (16.9 %)	19 (14.0 %)	5 (9.8 %)	11 (13.3 %)	16 (11.9 %)
Heavy pigm	6 (11.8 %)	3 (3.6 %)	9 (6.7 %)	7 (13.7 %)	3 (3.6 %)	10 (7.5 %)

were confirmed by *Regan & Rousseau* (1966) and they concluded that "retinal detachment may occur in eyes in which the rate of aqueous flow and also the facility of outflow are primarily abnormal and that the detachment is not necessarily the cause of the altered hydrodynamics". An imbalance was suggested in the physiology of aqueous production and the normal mechanisms of outflow and absorption and this imbalance was found to be bilateral in some cases even if the detachment occurred only in one eye.

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Group B This group consists of 37 patients (16 males and 21 females) with an average age of 57.3 years (17-109). As judged by the result of the Student's *t* test ($t = 1.996$, $0.05 < P < 0.10$) there is no significant difference in average age for females (61.1 years) and males (51.8 years).

7 of the males (43.8%) and 2 of the females (9.5%) were myopic and of these 3 males and 1 female exceeded minus 8.

Group A patients were hospitalized during 1967-1968 and group B patients during 1969. All patients included in this investigation had primary retinal detachment (unoperated) in one eye and the other eye was apparently healthy.

on 223 (105 males 118 females) detachment eyes and on 209 (97 males 112 females) fellow eyes. Four detachment eyes (aphakia - 2 aphakia and uveitis - 1 uveitis - 1) and eighteen fellow eyes (apparently normal eye - 2 enucleated - 1 previous perforating injury - 3 previous uveitis and phthisic bulb - 6 complicated cataract - 1 previously operated detachment - 3 uncomplicated cataract - 2) were not gonioscopically examined. The majority of these eyes were greatly pathological and in some of them gonioscopy was impossible to perform. Pathologic chamber angle would be expected in most of these eyes.

The results from the selected material (material III) are listed in table VIII.

Chamber angle width. Both table VII and VIII show open chamber angle (Grade IV + III) in almost 100 % of detachment eyes and fellow eyes. In table VII, one male eye is listed as closed angle. This eye had a serious contusion with hyphaema, iris dialysis, traumatic cataract followed by closed angle secondary glaucoma and finally retinal detachment.

Chamber angle pigmentation. In male detachment eyes and fellow eyes there is a higher incidence of heavy pigmentation than in the corresponding female groups (table VII and VIII). A higher incidence of heavy pigmentation (both sexes) is also seen in detachment eyes compared to fellow eyes (table VII). If all eyes harbouring complicating disorders (table II, III, V) are excluded, however, the higher incidence of heavy pigmentation in detachment eyes is eliminated.

Chamber angle ruptures. 9.5 % of the male and 2.5 % of the female detachment eyes harbour these changes. All these patients reported ocular contusion prior to detachment.

In table IX is listed a summary of some factors considered to be of importance when dealing with patients with some sort of trauma in predetachment history. The table is based on the case history, the type and severity of trauma and the result of gonioscopy and biomicroscopy (three mirror lens) in each traumatic case from material II. Biomicroscopy was not performed in 3 fellow eyes (enucleated - 1 cataract - 1 child lack of cooperation - 1).

Comment

A male prevalence in retinal detachment materials is the usual finding (Schepens & Marden 1961) but equal distribution among the sexes or female preponderance (Edmund 1964) has also been reported. A slight female prevalence (52.1 %) is seen among our total number of patients with retinal detachment in the two year period. When using the census population as basis it is however a statistically significant male prevalence in the age groups from 30-49 years. The male overrepresentation in these groups may partly be due to the higher

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By using fluorescein technique and suction cup *Dobbie (1963)* found evidence of decreased formation of aqueous humor in detachment eyes. These results

incidence of trauma among the males but other sex differences are possibly also of importance. The female prevalence observed in the higher age groups of retinal detachment patients is not statistically significant due to the corresponding change in ratio females to males in the general population. The average age for males is 6.6 years younger than for females and the female concentration in the higher age groups is more prominent than the male.

The effect of senescence is however seen in both sexes where the age group from 60-69 years comprises the highest number of patients. This can also be illustrated by the estimated ratio of inhabitants per one detachment per year. The calculation is possible due to the small number of eye departments in Norway and because the average number of retinal detachments treated each year in these departments is roughly known. The incidence in the age groups varies as expected greatly from 1 detachment per about 80 000 inhabitants (0-19 years) to 1 detachment per about 4000 inhabitants (60-69 years) per year. Similar results have been reported by *Bohringer* (1950) who also found the highest incidence in the age groups from 60-69 years.

The data obtained concerning age and sex relationship among the patients with retinal detachment from our department are in very good accordance with the data given by *Schepens & Marden* (1961 and 1966).

Material II includes 85% of the total number of patients with retinal detachment from our department over a two year period which were personally examined by the author. It is not likely that this selection has induced major differences in the results since the composition of material II is very close to the basic material from which it is extracted.

Bilateral detachment is in material II seen in 7.5% of the patients. The incidence varies in the literature but is given from Scandinavia by *Tornquist* (1963) - 15.5%, *Edmund* (1964) - 9.5%, *Braathen* (1968) - 5.1%.

Aphakic detachments range from 7 to 25% in series of retinal detachment (*Norton* 1964) and it is commonly accepted that aphakia gives increased risk towards retinal detachment. The incidence of aphakia among detachment eyes (11.9%) and fellow eyes (4%) in material II support this view. The difference is statistically significant at the 1% level, a fact which actually proves the increased risk.

Pseudoexfoliation of the lens capsule is found in 3.1% of detachment eyes and in 4% of fellow eyes. All patients (10) in which pseudoexfoliation was seen belong to the age groups over 60 years (125 patients) giving an incidence of 8%. This is in accordance with *Aasved's* (1969) incidence of pseudoexfoliation in normal populations over 60 years. The presence of pseudoexfoliation of the lens capsule will therefore not indicate any increased risk to retinal detachment.

Glaucoma diagnosed and treated prior to admission was seen in 4.4% of all patients in material II with no difference between detachment eyes (3.5%)

each time to avoid inexactitude which arises when using Friedenwald's nomogram

The time since detachment occurred (group A) was determined as exactly as possible in days based on the information given to the author by each patient. A Haff Planimeter 315 was used on the drawing made from each detachment eye and the detached area in per cent of the total area was calculated. The purpose of using this method was of course only to give a rough measure and not the exact area since it is impossible to transfer the fundus of an eye to a plane surface in this way.

All eyes were examined with the indirect ophthalmoscope (Schepens type) and the three mirror Goldmann lens but it is only the results (number of ruptures) from group A that are dealt with (in connection with hypotony of the eyes) in this paper.

Results

Group A Table I shows the distribution of eyes with intraocular pressure higher in detachment eye than in fellow eye (12.9%) equal intraocular pressure both eyes (27.4%) and lower intraocular pressure in detachment eye than in the other eye (59.7%). There is no major difference between the sexes in this distribution.

Table II shows the intraocular pressure in mm Hg (arithmetic mean in detachment eyes and fellow eyes). Intraocular pressure in fellow eyes is 1.98 mm

Table I

Group A Intraocular pressure (Schiotz tonometry) in detachment eye higher than in the fellow eye, equal intraocular pressure both eyes and lower intraocular pressure in detachment eye than in the fellow eye in per cent of number of eyes in males (46 patients), females (78 patients) and total (124 patients)

	Intraocular pressure		
	higher in detachment eye than in fellow eye	equal in both eyes	lower in detachment eye than in fellow eye
Males	10.9%	26.1%	63.0%
Females	14.1%	28.2%	57.7%
Total	12.9%	27.4%	59.7%

Table IX

Summary of some of the factors considered to be of importance among the traumatic cases from material II
 N = 36 (males = 27 females = 9)

	Detachment eyes							Fellow eyes						
	No of eyes with							No of eyes with						
	Number of patients	Angle lesion	Retinal degenerat	Oral dialysis	Arrow head rupt	Round holes	Prev ret detach	Family detach	Myopia	Posterior vitr detach/ vitr degenerat	Retinal degenerat	Prev ret detach	Arrow head rupt	Round holes
Perforating injury	+	1		1		1				1	1			
	++	4		3						2	2		1	
Ocular	+	10	4	8	4	3	4	1	3	6	7			
	++	6	4	3	2	4				4	3			
	+++	7	5	2	4	1	2			3	2			1
Indirect trauma		9		6	1	6	5	1	2	5	4	3	1	

There has been no previous surgery or injury, no previous diagnosed glaucoma or inflammation neither to the eyes with detachment nor to the fellow eyes. Gonioscopy revealed wide open chamber angle in all eyes.

Methods

All patients were examined by the author. Tonometry was performed with the same certified Schiötz tonometer on all eyes in group A and with another certified Schiötz tonometer on all eyes in group B. The same applanation tonometer (Goldmann's model Haag-Streit) was used on all patients in group B. Applanation tonometry was performed in the sitting position immediately followed by Schiötz tonometry in the lying position using 5.5 Gm plunger weight.

Tonometry in group A was performed before any mydriatics or cycloplegics were given and before any procedure was done which could alter intraocular pressure. However, some detachment eyes had received atropine by the referring ophthalmologists but usually the time between instillation of atropine and tonometry exceeded 24 hours. Group A patients came walking to the examination room and were examined the first day upon admission.

Group B patients had all both eyes dilated by topical instillation of Cyclogyl 1% (Cyclopentolate hydrochloride) and metaoxedrin hydrochloride 10% at least 30 minutes before tonometry. These patients were lying in bed with binoculars and were transported to the examination room in the bed. They were all examined the day after admission.

The differences in tonometry procedure and use of mydriatics in group A and B were partly the result of local circumstances; however, all patients in each group were examined under the same conditions.

Corneal anesthesia was obtained by topical use of oxibuprocaine 0.2%.

Intraocular pressure in mm Hg was taken from Friedenwald's 1955 table using the nearest 0.5 scale reading on the Schiötz tonometer. Applanation values were read to the nearest 0.5 mm Hg. Readings were taken from right eye - left eye until a constant value was obtained (approximately 2-4 readings each eye).

Ocular rigidity was calculated with the formula

$$K = \frac{\log P_t - \log (\text{appl ton} + 1)}{V_c \cdot 0.44}$$

(Ytteborg 1960). K = rigidity coefficient. P_t = intraocular pressure during tonometry (Friedenwald's 1955 table). V_c = volume of corneal indentation during Schiötz tonometry (Friedenwald 1955) and 0.44 mm^3 = corneal indentation caused by applanation tonometry (Goldmann & Schmidt 1957). K was calculated

to detachment, but an accident can also be proven by the presence of the anterior chamber angle lesions seen in the present study in 55.6% of male (60% of female) detachment eyes in which there has been a history of contusion. Tonjum (1966) found traumatic chamber angle ruptures in 94.3% of eyes with primary traumatic hyphaema. Since the incidence in the present study is not so high some of the contusions reported must have been of a minor degree. A detection of retinal dialyses will also point toward a traumatic genesis. This view is supported from the present study in which dialyses were found in 4.7% of the nontraumatic and in 36.1% of the traumatic detachment eyes.

When considering trauma (perforating injuries, ocular contusions, indirect trauma or combination of these) as cause to retinal detachment it is necessary to have in mind: 1. The severeness and type of the actual trauma. 2. The known disposition of the patient to retinal detachment (family, bilateral). 3. The disposition of the patient's eyes to retinal detachment (judged after a thorough examination including biomicroscopy, both eyes). As to the last point, the pre-existing condition of the detachment eye is usually not detected, but an examination of the fellow eye will give useful information about predisposing factors. It will be seen from table 1A that even in the perforating injury group (average age 27.6 years) the fellow eye is not healthy. Only one eye in this group was considered to be without predisposing factors. In the ocular contusion and indirect trauma groups four fellow eyes were considered healthy. These results support the view that traumatic retinal detachment is rare in a healthy eye (Gruber 1963).

The present investigation has shown a definite relationship between aphakia and retinal detachment and between chamber angle ruptures and retinal detachment. No such relationship has been proved for previously diagnosed glaucoma or uveitis.

Conclusions

1. The incidence of pseudoexfoliation is equal in detachment eyes and fellow eyes and the same as expected in a normal population within the same age groups.
2. Angle pigmentation is found to be of the same degree in detachment eyes and fellow eyes when eyes harbouring complicating factors are excluded.
3. Gonioscopy has revealed wide open chamber angle in nearly 100% of detachment eyes and fellow eyes.
4. Diagnostic mydriasis in these patients will not produce acute closed angle glaucoma.

Table III

Group A. Intraocular pressure (i.o.p.) in fellow eyes and detachment eyes (mm Hg Schiotz) area of detachment (in per cent of a total retinal detachment) in relation to duration of detachment in days N = number of patients in each group

Duration in days	i.o.p. detachment	i.o.p. fellow	difference	% detachment	N
1	15.80	15.54	+0.26	44.04	5
2	15.92	16.64	-0.72	53.31	3
3	13.53	14.83	-1.25	44.33	4
4	10.97	12.0	-1.08	49.33	10
5	10.01	15.12	-5.11	60.94	10
6-7	10.94	13.43	-2.49	55.94	11
8-9	10.59	13.59	-3.00	49.06	9
11-12-13	9.86	10.44	-0.58	61.0	7
14	9.35	12.35	-3.00	69.16	12
15-20	11.72	12.88	-1.17	60.50	8
21-29	10.92	12.25	-1.33	74.56	11
30-60	12.72	14.05	-1.33	63.36	13
61-180	11.10	13.35	-2.25	0.20	15
210-720	13.05	13.23	-0.18	70.90	6

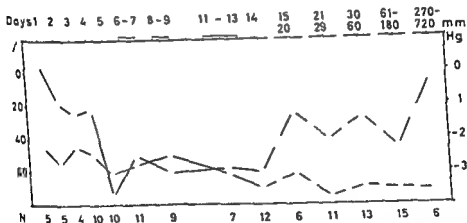


Fig 1

Table III is visualized in this figure X—X Average difference in intraocular pressure between detachment eyes and fellow eyes — Average area of detached retina.

Ruptures or holes in detached retina were found in approximately the same degree whether the detachment was fresh or longstanding. There was not found any relationship between degree of hypotony and number of ruptures. In 5 eyes

and fellow eyes (3.1%) Between 1 and 2% of the population over the age of 40 may have glaucoma (for references see *Duke-Elder* 1969) and the incidence increases with age According to this the incidence of glaucoma among the detachment patients is not especially high and the concept that glaucoma (or treatment with miotics) may cause retinal detachment is not supported

The *anterior chamber angle* has been found wide open in nearly 100% of all examined eyes with no difference between the sexes The anterior chamber is generally deeper in males than in females (*Tornquist* 1953) but the depth has not been measured in the present study and the difference between the sexes is therefore not ruled out Another factor considered to be of more importance to the present results of chamber angle width, is the possible effect of cycloplegia Gonioscopy has in all eyes been performed under mydriasis The cycloplegic effect of Cyclogyl will make the anterior chamber deeper (*Busacca* 1955) and increase chamber angle width due to decrease in ciliary body size backward movement of iris and flattening of the lens surface This effect has been noticed by the author in some eyes where gonioscopy was performed before and after mydriasis was obtained

The degree of widening of the anterior chamber angle has however not systematically been evaluated but is not thought to be of a magnitude that would cause considerable change in the results from the present study

The concept is therefore given that wide open chamber angle is a usual finding among patients suffering from retinal detachment No case of acute closed angle glaucoma has been seen or precipitated among these patients and mydriatics may thus be used in detachment eyes with little or no risk of angle closure It could also be suggested that patients with shallow angle or closed angle glaucoma are less prone to develop retinal detachment than patients with deep anterior chamber and wide open anterior chamber angle This is in agreement with *Cibis* (1965) hypothetical combinations of various sizes of the eye versus various sizes of the hyaloid body and the disposition to retinal detachment

Angle pigmentation No major difference in degree of pigmentation is found between detachment eyes and fellow eyes As expected the degree of pigmentation is reduced when eyes harbouring complicating factors are excluded A difference is however seen between male and female eyes in the heavy and moderate pigmentation groups but whether this difference is real or only a result of inaccuracy in estimating the degree of pigmentation is not clear

Trauma Retinal detachment due to trauma most commonly is seen in males (*Thiel & Kilian* 1963 *Cox et al* 1966) and this is significantly shown also in the present study

The time interval between trauma and detachment varies (table IV) but a long interval does not exclude trauma as possible cause When there has been a perforating injury there is seldom any question about trauma being the cause

Hg higher (average) than in detachment eyes This difference is significant (judged by the Student's *t* test which also will be applied to results later on $t = 6.831$ $P < 0.001$) There is also a significant difference (2.1 mm Hg) between female and male detachment eyes ($t = 2.831$ $P < 0.01$) and between female and male fellow eyes (1.19 mm Hg $t = 1.991$ $P < 0.05$)

In table III are listed average intraocular pressure and difference between fellow eyes and detachment eyes in relation to days duration of detachment The corresponding average area of detached retina in each group is tabulated and fig. 1 visualizes the results

The average area of detached retina is seen to increase rapidly the first days after occurrence of detachment then is followed by a more slow increase as time pass on

The average hypotony in detachment eyes compared to fellow eyes is most pronounced from 5 to 14 days after the occurrence of detachment After this time hypotony is reduced

Table IV will also illustrate the distribution of detachment eyes with intraocular pressure higher equal to and lower than the fellow eyes in three groups in relation to duration of detachment The differences (mm Hg arithmetic mean) between fellow and detachment eyes are listed in table V Between 5 and 14 days duration this difference is highly significant ($P < 0.001$) None of the other differences reach the 5% level of significance

The area of detached retina over 15 days duration is significantly greater than the area up to 14 days duration ($P < 0.005$)

It is thus shown that hypotony is greatest from 5 to 14 days after the occurrence of detachment and that area of detachment is greatest in cases with 15 days duration or more A direct relationship between area of detachment and degree of hypotony has not been found

Table II

Group A Intraocular pressure (I o p = arithmetic mean in mm Hg Schiotz) in detachment eyes and fellow eyes N = number of eyes s d = standard deviation of population

	Detachment eyes			Fellow eyes		
	Males	Females	Total	Males	Females	Total
N	46	78	124	46	78	124
I o p	10.22	12.32	11.54	12.71	13.96	13.52
s d	4.186	3.654	3.976	3.395	3.115	3.222

- Sebestyen J G Schepens C L & Rosenthal M L Retinal detachment and glaucoma. Arch Ophthal 61 736 745 1962
- Statistical Yearbook of Norway 81th issue III Central Bureau of Statistics of Norway Oslo 1963
- Thiel P & Kilian H Statistische Untersuchung über die Häufigkeit von Netzhautablosung nach stumpfen Trauma und die Notwendigkeit medizinischer Dokumentation. Klin. Monatsbl. Augenheilk. 143 564 576 1963
- Tonjum A Gonioscopy in traumatic hyphema. Acta Ophthal (khh) 44 650 664 1966
- Tornquist R Shallow anterior chamber in acute glaucoma Acta Ophthal (khh) Suppl 39 38 9 1953
- Tornquist R Bilateral retinal detachment. Acta Ophthal (khh) 41 126-133 1963
- Wolff S M & Zimmerman L E Chronic secondary glaucoma Am J Ophth 54 541 567 1967
- Zeege P Boyd T A W & Stewart A G Angle pigment in normal and chronic open angle glaucomatous eyes Canad J Ophthal. 16 505 511 1966

Table 1

Group A Difference between intraocular pressure in detachment eyes and fellow eyes (Schiotz) in relation to duration of detachment (in days) Area of detachment (in per cent of a total retinal detachment) in the groups and t values (Student's t test) Significance levels
N = number of patients

N	Duration in days	Difference	t value	sign level	Area of detachment	t value	sign level
94	0-4	-0.76	0.64	-	48.7%	3.134	1 < 0.001
49	5-14	-2.97	4.371	P < 0.001	58.3%		
30	15-60	-1.56	1.600	-	60.2%		
21	61-	-1.65	1.419	-	69.7%		

lation to the active lesion. Such extracellular virus particles were not found in the clinically undamaged areas of the corneal epithelium studied in the present investigation.

Discussion

Identification of structures as being virus particles was done on the basis of following facts: 1. The structures were similar in morphology to herpes simplex virus of known strain studied in tissue cultures (13-15). 2. The structures were found mainly within the cell nuclei. The DNA containing core (5) of herpes simplex virus is known to replicate within the nucleus (3, 11, 13). Although normal cytoplasmic structures may sometimes resemble virus particles, normal nuclei never contain such structures. 3. For one of the patients isolation of virus as well as serological tests were performed. Both ways the presence of an infection with herpes simplex virus was proven. The purpose of the present investigation was to study the distribution of virus particles in human corneal epithelium by comparing areas with active lesions to clinically undamaged areas. Previous work on rabbit corneal epithelium (7, 17, 18) was based on inoculation experiments and is not likely to reflect the situation in human after spontaneous infection. A precise knowledge of the location in relation to the active dendritic lesions of the biopsies taken is essential. This was made possible by carefully dissecting out strips of corneal epithelium under visual control in the split lamp microscope. Scraping the cornea in order to obtain minimal flakes of tissue (14) is in this respect unsatisfactory. An improvement of the tissue preservation as compared to that of an earlier study of human dendritic keratitis (16) also contributed to the possibility of a more precise analysis of the cells involved.

In a previous report on dendritic keratitis (14) and in the present paper it has been shown that virus particles may be present in a very large number of cells in undamaged areas of the corneal epithelium. The lack of enveloped extracellular virus particles, the very low number of virus particles in the cytoplasm and the fairly low number of intranuclearly located virus particles as compared to the picture of the dendritic lesion are indications that the infection might be of different degree of activity in different areas of the corneal epithelium. It seems that the rate of replication of virus particles is very high in the dendritic lesions and very low or perhaps absent in other areas. This finding is in agreement with other evidence in the literature that herpes simplex virus might lie dormant in the tissue. Kaufman, Brown & Ellison (8) studied sections of lacrimal gland and conjunctiva with fluorescein-labelled antibody to herpes simplex virus and showed that virus antigen was present in four of seven

Table IV

Group A Intraocular pressure (Schiotz) in detachment eye higher than in the fellow eye equal intraocular pressure in both eyes and lower intraocular pressure in detachment eye than in the fellow eye in relation to duration (in days) of detachment Average area of detached retina (in per cent of a total retinal detachment) in each group

N = number of patients

N	Duration in days	Intraocular pressure			Area of detachment
		higher in detachment eye than in fellow eye	equal in both eyes	lower in detachment eye than in fellow eye	
24	0-4	25 %	29.2 %	45.8 %	48.1 %
49	5-14	6.1 %	24.5 %	69.4 %	58.3 %
51	15-	15.7 %	47 %	37.3 %	69.7 %

no rupture or hole in detached retina was detected. The average hypotony in these eyes were 2.8 mm Hg.

Group B The results concerning ocular rigidity and intraocular pressure (applanation and Schiotz tonometry) are listed in table VI. Ocular rigidity is insignificant lower in detachment eyes than in fellow eyes. A significant difference is seen between ocular rigidity in females and males both in detachment ($t = 2.230$ $P < 0.05$) and fellow ($t = 2.394$ $P < 0.05$) eyes.

As found in group A, intraocular pressure in detachment eyes generally is lower than in fellow eyes. The number in group B are however too small to yield significance.

The average applanation values are higher than the Schiotz values. The difference in detachment eyes is 1.23 mm Hg and in fellow eyes 1.05 mm Hg.

Comment

Both group A and B consists of patients selected from our department. The aim has been to reduce factors with possible influence on intraocular pressure as much as possible, therefore only paired eyes without any other known disorder besides retinal detachment in one eye are used.

Among retinal detachment patients the average age for females is usually higher than for males (Schepens & Marden 1961, Syrdalen 1970). This is also the situation in group A and B.

Intraocular pressure Retinal detachment is usually associated with hypotony

Table II

Intraocular pressure (P_o) in mm Hg in fellow eyes and operated detachment eyes in groups in relation to time after operation N = number of patients in each group Numbers in brackets = standard deviation of population

Method of operation	Interval since operation (days)	N	Applanation tonometry				Schiotz tonometry			
			P_o fellow eyes	P_o detach eyes	P_o fell - P_o detach	t value* sign level	P_o fellow eyes	P_o detach eyes	P_o fell - P_o detach	
Group A Encircling procedures	9- 14	9	15.33 (1.23)	10.56 (3.58)	4.77	4.560 $P < 0.005$	13.61 (2.01)	2.79 (2.05)	10.82	
	19- 54	9	14.50 (3.83)	10.33 (2.66)	3.67	2.507 $P < 0.05$	13.41 (3.96)	3.88 (1.89)	9.53	
	61-1020	24	14.77 (3.25)	12.83 (3.93)	1.94	2.747 $P < 0.02$	14.59 (2.46)	5.47 (3.97)	9.12	
	total	42	14.85 (3.02)	11.92 (3.70)	2.93	5.082 $P < 0.001$	14.13 (2.74)	4.56 (3.41)	9.57	
Group B Local buckling procedures	10- 33	5	13.60 (2.30)	11.20 (1.48)	2.40	3.359 $P < 0.05$	14.71 (2.41)	7.63 (1.78)	7.03	
	69- 150	8	15.00 (3.57)	13.38 (2.49)	1.62	1.713 -	14.19 (3.07)	11.37 (2.32)	2.82	
	total	13	14.46 (3.12)	12.54 (2.36)	1.92	3.065 $P < 0.01$	14.39 (2.74)	9.95 (2.77)	4.44	

* Method of paired comparison employed by testing the results from fellow eyes against detachment eyes

ous production and that the greatest reduction could be found if eyes with detachment of 5 to 14 days duration were examined. The hypotony may be caused by an aqueous production shock which it takes some days to see the result of and which lasts for about ten days at maximum. Afterwards aqueous production to a certain extent is regained but as hypotony persists other factors of influence on ocular hydrodynamics still may be present.

Ocular rigidity. No significant difference is found between detachment eyes and fellow eyes and this is in agreement with results reported by Ytteborg (1961), Rousseau & Regan (1965) and Regan & Rousseau (1966). In the present study there is however a difference in ocular rigidity between males and females. This difference is probably due to the high percentage of myopic patients in the male group as ocular rigidity decreases with increasing degree of myopia (Castren & Pojola 1962). Average age and intraocular pressure is higher in females than in males. This may have reduced the difference in ocular rigidity between males and females a little since ocular rigidity will decrease with increasing age (Ytteborg 1960a) and with increasing intraocular pressure (Ytteborg 1960b).

Fellow eyes. An interesting result of the present investigation is the low average intraocular pressure in all fellow eyes. Graham & Hollows (1964) found average Schiotz pressure in males (age 50 to 64 years) to be 14.5–14.6 mm Hg and in females (same age) to be 15.8–15.9 mm Hg. They also found applanation values in average to be 1 mm Hg higher than Schiotz values. The average intraocular pressure in fellow eyes (group A and B) in the present study varies from 2 to 3.5 mm Hg below these normal values. The reason to this rather low pressure is not quite clear. It may be a support to the statement from Regan & Rousseau (1966) that an imbalance in the physiology of aqueous production and the normal mechanisms of outflow and absorption exists in these patients.

The use of mydriatics in group B is not the reason since the same result is seen in group A where no mydriatics were used. However mydriatics in group B may have had some influence on intraocular pressure since the difference between average group A (13.52 mm Hg) and B (11.95 mm Hg) is significant ($t = 2.608$, $P < 0.01$). It is also possible that the difference in examining procedure (walking patient group A, patients lying in bed group B) may be of some importance in this respect.

Applanation Schiotz values. It is usual to find that applanation tonometry yields higher values than Schiotz tonometry (using Friedenwald's 1955 table) (Laufer Smith 1961). Graham & Hollows (1964) found the difference to be about 1 mm Hg and the same has been found in the present study. The change from sitting to lying position will induce a rise in intraocular pressure from 1 to 2 mm Hg (or even more) (for references see Helander-Erikson 1966). The values for intraocular pressure given in Friedenwald's 1955 table must therefore be too low compared to the applanation values and the difference has been shown

ration, average 253 days) and in group B (examination from 69 to 150 days after operation, average 113 days)

Comment

In the present investigation the fellow eyes serve as controls. A comparison of the results is only valid between detachment eyes and corresponding fellow eyes and not between the detachment eyes in the different groups as the numbers are small and differences in age, sex and refraction will give such a comparison limited value.

Ocular rigidity. Sources previously referred to have shown that different forms of ocular surgery leads to reduced ocular rigidity. The decrease in h may be reversible (Lavergne 1959) and this view is supported by the results from the present study (group B). In these eyes the destruction on the eye wall is restricted to a limited area. As postoperative ocular hyperemia (which in itself produces reduction in h (Ylfeborg 1960)) disappears and reparative mechanisms are finished, ocular rigidity increases again. In group A, however, the reduction in h is permanent. h is extremely low in the first postoperative period and continues to stay low even if a small raise is seen. Postoperative ocular hyperemia and reparative mechanisms may influence h in group A as in group B but the main reason to the permanently very low h in group A is believed to be the encircling element per se.

The cerclage produces a permanent disconfiguration of the eye which leads to a decrease in intraocular volume. During Schiøtz tonometry a certain volume is indented in the cornea and a deformation of the posterior part of the eyeball takes place. The volume of fluid displacement brought about in this way (V_i) (for references see Hetland Eriksen 1965) is normally made room for by distension of the eye walls by expulsion of blood from the choroid and by aqueous outflow. In cerclage operated eyes part of V_i may be given room for by the volume increase (ΔV) an elongation of the cerclage (ΔC) will produce as the intraocular pressure goes from P_0 (intraocular pressure before tonometry) to P_1 (intraocular pressure while the tonometer rests on the eye). ΔV will add to normal mechanisms which serve to give room for V_i . In this way higher scale readings are obtained on the Schiøtz tonometer demonstrating a decrease in ocular rigidity. Mathematically ΔV may be calculated using the model eye shown in fig. 1 and the volume within the cerclage cylinder. If $h = 3$ mm and $r_1 = 9$ mm $\Delta V = 0.2353 \Delta C^3 + 27 \Delta C$. Fig. 2 demonstrates the relationship between ΔV and ΔC .

Intraocular pressure. The low ocular rigidity in these eyes leads to erroneous results if scale reading Schiøtz is converted into mm Hg intraocular pressure

Table VI

Group B Ocular rigidity (K) applanation (Appl) and Schiötz (Sch) tonometry (mm Hg) in males females and total Detachment eyes and fellow eyes N = number of patients s d = standard deviation of population

	Detachment eyes			Fellow eyes		
	males	females	total	males	females	total
N	16	21	37	16	21	37
K	0 0154	0 0187	0 0173	0 0164	0 0194	0 0181
s d	0 0045	0 0045	0 0045	0 0032	0 0045	0 0045
Appl	12 50	11 62	12 0	12 88	13 10	13 0
s d	5 09	4 26	4 59	2 85	3 59	3 75
Sch	10 26	11 15	10 77	11 0	12 67	11 95
s d	4 63	3 76	4 12	2 88	3 32	3 91

(Kleiner 1933 Huerfamp & Behme 1955 Ytteborg 1961 Becler 1963 Dobbie 1963 and many others) and the present investigation has only confirmed this

The hypotony is usually moderate the first days after the occurrence of detachment (fig 1) between 5 and 14 days it is at maximum and after this time it subsides gradually This finding concerning the older detachments is in agreement with *Sebestyen et al* (1962) who found that postoperative elevation of ocular pressure was related to duration of the retinal detachment and that longstanding cases may have a tendency toward glaucoma In the present series of retinal detachment there has however not been detected any cases of glaucoma neither in fresh nor in older detachments

Kleiner (1933) and Dobbie (1963) found increasing hypotony with increasing size of retinal detachment and Kleiner did also notice that the hypotony was less marked the first days after the occurrence of a detachment than afterwards To some degree the present investigation show similar results but it has been shown (fig 1) that there is not a direct relationship between average area of detachment and average degree of hypotony The hypotony follows some days after the occurrence of detachment and decreases after a period at maximum even if area of retinal detachment gradually increases as time pass on

The present study has not shown any direct relationship between number of retinal holes or area of detachment and hypotony of the eye Decreased formation of aqueous humor has already been shown to exist in detachment eyes (Dobbie 1963 Becler 1963 Regan & Rousseau 1966) but the present study would indicate that there might be considerable variation in the rate of aque

Table II

Intraocular pressure (P_o) in mm Hg in fellow eyes and operated detachment eyes in groups in relation to time after operation N = number of patients in each group Numbers in brackets = standard deviation of population

Method of operation	Interval since operation (days)	N	Appplanation tonometry				Schiotz tonometry		
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* Method of paired comparison employed by testing the results from fellow eyes against detachment eyes

References

- Becker B Discussion after J Lawton Smith Retinal detachment and glaucoma Trans Amer Acad Ophthal Otolaryng 67 731 1963
- Beigelman M V Acute hypotony in retinal detachment Arch Ophthal 1 463 467 1959
- Cautren J A & Pajola S Myopia and scleral rigidity Acta Ophthal (Abh) 40 33 36 1962
- Danziger M The difference in ocular pressure in the two eyes of the same person Acta Ophthal (Abh) 43 299 313 1965
- Dobbie J G A study of the intraocular fluid dynamics in retinal detachment Arch Ophthal 69 139 164 1963
- Goldmann H & Schmidt Th Über Applanationstonometrie Ophthalmologica 134 91 97 1957
- Graham P & Hollous F C Sources of variation in tonometry Trans Ophthal Soc U K 84 597 631 1964
- Guillaumat L & Bonnin P Decollement de la rétine et hypertension Probl actuels Ophthal 9 93 113 Karger Basel/New York 1967
- Helland Eriksen J On tonometry 6 Comparative tonometry with the Goldmann applanation tonometer and the Schiotz tonometer in the lying position. Acta Ophthal (Abh) 44 572 588 1966
- Huerkamp B & Behme H Die Augendrucklage insbesondere das Glaukom bei Ablatio retinae mit Oratiss V Graefes Arch Ophthal 106 439 442 1955
- Kleiner L Der intraokulare Druck bei Netzhautablösung V Graefes Arch Ophthal 119 435 500 1933
- Lawton Smith J Retinal detachment and glaucoma Trans Amer Acad Ophthal Otolaryng 67 796-731 1963
- Lawton Smith J The incidence of Schiotz applanation disparity Cooperative study Arch Ophthal 7 305 309 1967
- Regan C D J & Rousseau A P The intraocular dynamics of eyes with retinal detachment Am J Ophth. 61 696- 07 1966
- Rousseau A P & Regan C D J Pressure cup studies in eyes with retinal detachment Arch Ophthal 73 803 809 1965
- Sarni L & Chesson G J & McDonald P R The problem of retinal detachment in the presence of glaucoma Am J Ophth 56 908 911 1963
- Schepens C L & Marden B A Data on the natural history of retinal detachment Arch Ophthal 66 631 647 1961
- Schepens J G Schepens C L & Rosenthal M L Retinal detachment and glaucoma Arch Ophthal 6 736 45 1962
- Syrdlen P Trauma and retinal detachment Acta Ophthal (Abh) in press 1968
- Titterton J Rigidity coefficient before and after diathermy coagulation of the sclera Acta Ophthal (Abh) 39 54 55 1961
- Titterton J The role of intraocular blood volume in rigidity measurements on human eyes Acta Ophthal (Abh) 38 410 436 1960
- Titterton J Further investigations of factors influencing size of rigidity coefficient Acta Ophthal (Abh) 39 643 657 1960a
- Titterton J The effect of intraocular pressure on rigidity coefficient in human eye Acta Ophthal (Abh) 39 548 561 1960b

tonometry is therefore strongly recommended for intraocular pressure assessment on operated retinal detachment eyes

Sources previously referred to have stated that reattachment of the retina fails to restore intraocular dynamics to normal. The results of this present investigation support this view.

Conclusions

- 1 Following retinal detachment surgery ocular rigidity (k) is reduced
- 2 Following local buckling procedures this reduction to some extent is reversible
- 3 Following encircling operations with silicone rubber band the reduction in k is permanent.
- 4 A small elongation of the encircling element will give room for an increased corneal indentation volume (Schiotz tonometry). This may indicate that the encircling element per se and the disconfiguration of the eye which is produced are the main reasons to the extremely low k .
- 5 Retinal detachment surgery is followed by hypotony of the eye (applanation)
- 6 This hypotony is gradually reduced with time after operation
- 7 Encircling procedure produces a more pronounced early postoperative hypotony than does a local buckling procedure
- 8 A large Schiotz - applanation disparity is seen in operated retinal detachment eyes.
- 9 Applanation tonometry is recommended to be used to assess intraocular pressure level in operated retinal detachment eyes

Summary

The results on ocular rigidity and intraocular pressure (Schiotz applanation) are presented for 55 successfully operated retinal detachment patients. Ocular rigidity is largely and permanently reduced following encircling procedures. Following local buckling procedures the low ocular rigidity to some degree is reversible. Hypotony is seen after retinal detachment surgery. The hypotony is reduced as time passes on after operation but intraocular pressure in detachment eyes will as a rule not reach the level of fellow eyes.

to be 5 mm Hg when both procedures were performed in the lying position (Hettland-Eriksen 1966)

Intraocular pressure females-males In group A a significant lower intraocular pressure was found in males than in females both in detachment eyes and fellow eyes Graham & Hollows (1964) found a similar difference but there is no obvious explanation to this fact Among the detachment patients the higher incidence of myopia among males may have some influence on the results but since ocular rigidity has not been calculated in this group the degree can not be established The difference in average age is too small to yield such a difference in intraocular pressure

Conclusions

- 1 Retinal detachment induce hypotony of the eye
- 2 The hypotony is most pronounced 5 to 14 days after the occurrence of detachment and then decreases
- 3 The hypotony is not proportional to area of detachment
- 4 The hypotony is not proportional to number of retinal holes
- 5 No difference is found in ocular rigidity between detachment eyes and fellow eyes
- 6 Average intraocular pressure in fellow eyes is 2 to 3.5 mm Hg lower than what expected in a normal population This may indicate altered hydrodynamics in the eyes of these patients even before detachment occurred
- 7 The average intraocular pressure in males is about 1 mm Hg lower than in females
- 8 Applanation values in sitting position are generally 1 mm Hg higher than Schiotz values in lying position This finding strongly indicate that the P_0 values listed in Friedenwald's 1955 table are too low

Summary

Two groups of retinal detachment patients without any other eye disorder neither in detachment eye nor in fellow eye are examined

Group A Relation between intraocular pressure area of detachment duration of detachment and number of retinal holes among 124 patients are dealt with

Group B Schiotz and applanation tonometry and ocular rigidity in 34 patients are dealt with

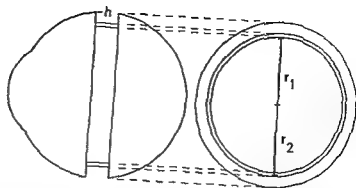


Fig 1

Schematic drawing of a cerclage operated eye in sagittal and frontal projection r_1 = radius of the circle made by the cerclage before tonometry r_2 = radius of the same circle during tonometry h = height (width of) the buckle made by the cerclage

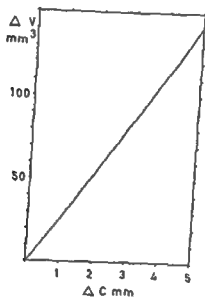


Fig 2

Volume increase (ΔV mm³) of cerclage cylinder (see text) corresponding to elongation (ΔC mm) of cerclage

using Friedenwald's 1955 table Applanation values may be several mm Hg higher than Schiötz values (table II) The results of applanation tonometry on eyes with very different ocular rigidity (such as the present results) are very little influenced by this difference due to the small volume of corneal indentation produced by this method (0.442 mm³ Goldmann & Schmidt 1957) and the corresponding small raise in intraocular pressure during tonometry Applanation

References

- Becker B Discussion after J Lawton Smith Retinal detachment and glaucoma Trans Amer Acad Ophthalmol Otolaryng 67 731 1963
- Beigelman, M V Acute hypotony in retinal detachment Arch Ophthalmol 1 463-467 1979
- Castren J A & Popola S Myopia and scleral rigidity Acta Ophthalmol (Abh) 40 33 36 1967
- Donanger M The difference in ocular pressure in the two eyes of the same person Acta Ophthalmol (Abh) 43 299 313 1965
- Dobbs J G A study of the intraocular fluid dynamics in retinal detachment Arch Ophthalmol 69 139 164 1963
- Goldmann H & Schmidt Th Ober Applanationstonometrie Ophthalmologica 134 242 1951
- Graham P & Hollows F C Sources of variation in tonometry Trans Ophthalmol Soc U K 84 597 631 1964
- Guillaumat L & Bonnin P Decollement de la retine et hypertension Probl actuels Ophthalmol 3 113 Karger Basel/New York, 1967
- Hertel Eriksen J On tonometry III Comparative tonometry with the Goldmann applanation tonometer and the Schiotz tonometer in the lying position. Acta Ophthalmol (Abh) 44 522 538 1966
- Huerkamp B & Behme H Die Augendrucklage insbesondere das Glaukom bei Ablatio retinae mit Orariss V Graefes Arch Ophthalmol 106 433 447 1965
- Kleiner L Der intraokulare Druck bei Netzhautablösung V Graefes Arch Ophthalmol 100 485 506 1943
- Lawton Smith J Retinal detachment and glaucoma Trans Amer Acad Ophthalmol Otolaryng 67 706-791 1963
- Lawton Smith J The incidence of Schiotz applanation disparity Cooperative study Arch Ophthalmol 1 303 308 1967
- Pease C D J & Rousseau A P The intraocular dynamics of eyes with retinal detachment Am J Ophthalmol 61 696 70 1966
- Rousseau A P & Regan C D J Pressure cup studies in eyes with retinal detachment Arch Ophthalmol 73 803 809 1965
- Serin L K Chessin G J & McDonald P R The problem of retinal detachment in the presence of glaucoma Am J Ophthalmol 56 909 911 1963
- Schepens C L & Marden B J Data on the natural history of retinal detachment Arch Ophthalmol 66 631 642 1961
- Schepens C L Schepens C L & Rosenthal M L Retinal detachment and glaucoma Arch Ophthalmol 61 736 45 1967
- Sjodalen P Trauma and retinal detachment Acta Ophthalmol (Abh) in press 19 0
- Sturberg J Rigidity coefficient before and after diathermy coagulation of the sclera Acta Ophthalmol (Abh) 39 541 550 1961
- Sturberg J The role of intraocular blood volume in rigidity measurements on human eyes Acta Ophthalmol (Abh) 38 410 416 1960
- Sturberg J Further investigations of factors influencing size of rigidity coefficient Acta Ophthalmol (Abh) 38 643 657 1960a
- Sturberg J The effect of intraocular pressure on rigidity coefficient in human eye. Acta Ophthalmol (Abh) 39 543 61 1960b

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CORNEAL INDENTATION PULSE AND RETINAL DETACHMENT PRE AND POSTOPERATIVE STUDY

BY

PER SYRDALEN

Hydrodynamically the vascular bed of the eye may be divided into a non pulsatile and a pulsatile part. The blood flows through the non pulsatile part at a constant volume per time unit in diastole and in systole while the pulsatile part receives blood in systole. This excess of blood entering the eye in systole will according to its volume (ΔV) and the intraocular pressure level initiate a corresponding increase in intraocular pressure (ΔP). Pulsessynchronous variations in intraocular pressure was first recognized by Weber in 1850 and may be studied in detail by various methods (Suuki 1962, Davanger 1963, Castren & Lavikainen 1963, Bynke & Krakau 1964, Bron et al 1967) of which dynamic tonometry (Horten 1968) is used in the present study.

Clinically the corneal pulse amplitudes will vary with the size of ΔV . Decrease in amplitudes is seen by occlusion of the common or internal carotid artery (Zitcborg 1960, Castren & Lavikainen 1963, Bron et al 1967) during general anesthesia (Horten & Syrdalen 1970) during retrobulbar anesthesia (Syrdalen & Horven 1970) during tachycardia (Horven & Syrdalen 1970) in giant cell arteritis (Horven 1970c) and in choroidal degenerations (Bynke & Schule 1967, Horten 1970b). Increase in corneal pulse amplitudes has been seen in Sturge Weber's syndrome (Flage & Horven 1970) during bradycardia (Horten & Syrdalen 1970) during pain attacks of cluster headache (Broch et al 1970) by arteriovenous shunts (Horten 1970b) by choroidal melanomas (Hor

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INTRAOCULAR PRESSURE AND OCULAR RIGIDITY IN PATIENTS WITH RETINAL DETACHMENT

II Postoperative study

BY

PER SYRDALEN

Retinal detachment is usually accompanied by hypotony of the eye (Klemer 1933 Syrdalen 1970) This hypotony is possibly the result of the decreased aqueous humor formation which has been shown to exist in these eyes (Dobbie 1963) It has also been shown that hypotony reduced aqueous humor formation and abnormally low outflow facilities are present in both eyes of many patients with unilateral nontraumatic retinal detachment. This suggest an underlying pathology common to both eyes which probably precede the detachment (Becker 1963 Rousseau & Regan 1965 Regan & Rousseau 1966 Langham & Regan 1969) This imbalance which exists in the physiology of aqueous formation and outflow facility in retinal detachment eyes will last after an operation Reattachment of the retina thus fails to restore intraocular dynamics to normal (Lozano Elionda & Schepens 1968 Bietti 1968)

Glaucoma may be seen in association with retinal detachment (Sebestyen et al 1962 Sarin et al 1963 Lawton Smith 1963) Usually factors present before detachment operation (previous ocular trauma glaucoma aphakia or uveitis) or complications following detachment surgery (choroidal detachment

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References

- Ally M A Rigiditätsänderung nach Operation der Netzhautablosung V Graefes Arch Ophthal 167 625 630 1964
- Becker B Discussion after J Lawton Smith Retinal detachment and glaucoma Trans Amer Acad Ophthal Otolaryng 67 731 1963
- Bietti G B in McPherson A (ed) New and controversial aspects of retinal detachment Hoeber Medical Division, Harper & Row New York p 492 1968
- Custodis E in Schepens C L (ed) Importance of the vitreous body in retina surgery The C V Mosby Company St Louis pp 145 182 1960
- Dobbie J G A study of the intraocular fluid dynamics in retinal detachment. Arch Ophthal 69 159 164 1963
- Draeger J Untersuchungen über den Rigiditätskoeffizienten Documenta Ophth VIII 431 486 1959
- Goldmann H & Schmidt T Über Applanations-tonometrie Ophthalmologica 134 221 242 1957
- Helander Eriksen J On tonometry 7 The volume of displaced fluid by Schiotz tonometry Acta Ophthal (Kbh) 44 725 736 1966
- Kleiner L Der intraokulare Druck bei Netzhautablosung V Graefes Arch Ophthal 129 485 506 1933
- Langham M E & Regan C D J Circulatory changes associated with onset of primary retinal detachment Am J Ophth 51 820 829 1969
- Lavergne G Les modifications post opératoires de la rigidité oculaire. Ophthalmologica 139 169 174 1959
- Lawton Smith J Retinal detachment and glaucoma Trans Amer Acad Ophthal Otolaryng 67 726 731 1963
- Lozano Elsonda & Schepens C L cited by Langham M E & Regan, C. D J Circulatory changes associated with onset of primary retinal detachment Am J Ophth 51 p 827 1969
- Pemberton J W Schiotz applanation disparity following retinal detachment surgery Arch Ophthal 51 534 537 1969
- Regan C D J & Roussseau A P The intraocular dynamics of eyes with retinal detachment Am J Ophth 61 696 702 1966
- Roussseau A P & Regan C D J Pressure cup studies in eyes with retinal detachment Arch Ophthal 73 803 809 1965
- Sarin L K Chesson G J & McDonald P R The problem of retinal detachment in the presence of glaucoma Am J Ophth 56 908 911 1963
- Schepens C L in McPherson A (ed) New and controversial aspects of retinal detachment Hoeber Medical Division Harper & Row New York pp 364 390 1968
- Sebestyen J G Schepens C L & Rosenthal M L Retinal detachment and glaucoma Arch Ophthal 67 436 445 1962
- Syrdalen P Intraocular pressure and ocular rigidity in patients with retinal detachment I Preoperative study Acta Ophthal (Kbh) in press 1969
- Weidenthal D T Retinal reattachment without release of subretinal fluid Am J Ophth 63 108 112 1967
- Ytteborg J The role of intraocular blood volume in rigidity measurements on human eyes Acta Ophthal (Kbh) 38 410 436 1960
- Ytteborg J Rigidity coefficient before and after diathermy coagulation of the sclera Acta Ophthal (Kbh) 39 547 550 1961

with closure of filtration angle goniosynechiae uveitis) may explain such a glaucoma.

A factor which may be of importance when dealing with postoperative intraocular pressure in retinal detachment eyes is the ocular rigidity (k = rigidity coefficient) k is not constant but differs little in the two healthy eyes of the same individual. Prior to retinal detachment operations there has not been found any difference in k between detachment eyes and fellow eyes (Ytteborg 1961 Aly 1964 Rousseau & Regan 1965 Regan & Rousseau 1966 Langham & Regan 1969 Syrdalen 1970) but different forms of ocular surgery including retinal detachment operations may lead to reduced k (Draeger 1959 Lavergne 1959 Ytteborg 1961 Aly 1964 Pemberton 1969).

In an earlier investigation (Syrdalen 1970) preoperative intraocular pressure (Schiotz tonometry and applanation tonometry) and ocular rigidity in detachment eyes and fellow eyes were studied. In the present investigation the postoperative course is studied.

Material and Methods

The present investigation took place during 1969. All patients included in this study have been hospitalized and operated in the eye department Rikshospitalet Oslo due to primary retinal detachment in one eye and with a fellow eye without retinal detachment. Prior to admission there had been no form of surgery neither to detachment eyes nor to fellow eyes. Cases with trauma in history glaucoma or uveitis are excluded. Only eyes successfully operated are included and all eyes had wide open anterior chamber angle visible by gonioscopy. The patients were examined at different intervals after operation (range from 9 to 1020 days) and all examinations were performed by the author. The criteria used in the selection of patients limited the total number.

The operation methods were local full thickness scleral buckling procedure encircling procedure (cerclage) or a combination of the two methods. Diathermy or cryosurgery were used to produce chorioretinal adhesions. Silicone rubber implant(s) were used to local buckling procedures usually without drainage of subretinal fluid (Custodis 1960 Weidenthal 1961). The encircling procedures were performed with a flat silicone rubber band of 2 mm width. The principles for this method including release of subretinal fluid as given by Schepens (for references see Schepens 1968) have mainly been followed. Eyes operated with scleral resection or trap door procedure or eyes treated solely with local diathermy or local cryosurgery procedure are not included in the present series.

The material is divided into two groups of patients according to the operation performed.

surgery alone. Chorioretinal adhesions had been obtained either with the use of diathermy (19 patients) or cryosurgery (20 patients)

19 patients were examined both pre and postoperatively and are thus included both in the pre and in the postoperative dynamic tonometry group

Methods

Dynamic tonometry is performed with the patient in supine position. The equipment consists of an electronic Schiotz tonometer, an amplifier unit and a recorder (for closer description see *Horven 1968*). The Schiotz tonometer yields an output of 1 mV per μ plunger movement. In the present study the 5.5 Gm plunger weight was used throughout. Eye tension in scale reading Schiotz was recorded (right eye - left eye) using sensitivity setting 20 mV and converted into mm Hg intraocular pressure using Friedenwald's 1933 table. Corneal indentation pulse amplitudes were recorded using sensitivity setting 2 mV (right eye - left eye) and 1 mV. Usually the size of the corneal indentation pulse amplitudes were calculated as an average of 5 to 10 representative waves. Corneal indentation pulse amplitudes (μ) were converted into mm^3 change in ocular volume (ΔV) at the actual intraocular pressure level using converting table based on Langham - Heiland Eriksen's data as given by *Horven (1970a)*.

Preoperative dynamic tonometry was performed on the day of surgery or from 1 to 8 days prior to operation. *Postoperative dynamic tonometry* was performed at an average of 121.5 days after operation (range from 7 days and up to 2 years). (In the cerclage group the interval between operation and dynamic tonometry was on average 157.8 days (range 7 to 480 days) and in the local buckling group 101.3 days (range 9 days and up to 2 years)).

In the present study dynamic tonometry was performed before any procedure was done which would alter intraocular pressure considerably. However both in the preoperative and in the postoperative examined patients some difference between detachment eyes and fellow eyes was present in the use of cycloplegics and mydriatics but this difference seems to have had very little influence on intraocular pressure and corneal indentation pulse amplitudes.

Results

In table 1 the results of pre and postoperative dynamic tonometry are summarized. The difference between detachment eyes and fellow eyes are statistically

Group A

Encircling procedure This group includes 42 patients with an average age of 57.5 years (range from 16 to 79 years). In this group 18 patients were operated with cerclage alone and 24 patients with cerclage plus circular or meridional silicone rubber implant(s).

Group B

Local buckling procedure This group includes 13 patients with an average age of 58.5 years (range from 39 to 70 years).

Tonometry (Schiotz and applanation) and calculation of rigidity coefficient (K) is performed as previously described (Sjrdalen 1960). The 5.5 Gm plunger weight on the Schiotz tonometer was preferred due to the fact that heavier weights gave scale readings over 20 in a great number of the cases.

Results

In table I and II a summary of the results is listed. The results obtained from those operated with cerclage and those operated with cerclage plus silicone rubber implant(s) were not significantly different. These cases are therefore put together in the tables as the encircling procedure group. Each patient is listed once even if two or more examinations are done postoperatively. The results from the latest postoperative examination are used in the tables.

Ocular rigidity A marked reduction in K is seen in all postoperative periods in group A. In group B K is also significantly reduced but this reduction is to a certain degree reversible. In group A 9 patients were examined on two different occasions. The first examination (from 9 to 45 days postoperatively average 16.4 days) gave K in detachment eyes = 0.0047 (s.d. = 0.0014). The second examination (from 30 to 155 days after operation average 93.7 days) gave K in the same detachment eyes = 0.0065 (s.d. = 0.0017). This increase in K is statistically significant (as judged by the method of paired comparison $t = 3.629$ $P < 0.01$). The corresponding K in fellow eyes on the first and second postoperative examination was 0.0212 (s.d. = 0.0034) and 0.0203 (s.d. = 0.0031).

Intraocular pressure (applanation) There is hypotony in all groups of detachment eyes after operation. The intraocular pressure is at the lowest level immediately after operation and the greatest hypotony is seen in group A. Hypotony is reduced as time passes on but is still present more than 60 days after operation both in group A (examination from 61 to 1020 days after ope

ven 1969) and by elevation to 40-50 mm Hg of intraocular pressure (Hörve 1970b)

The ocular rigidity (K = rigidity coefficient) is expected to be of importance to the size of corneal pulse amplitudes as suggested by Bron *et al* (1967) and Byrke (1968). The relationship between ΔP and ΔV with different size of K has been illustrated by Davanger (1964) in his mechanical model of an eye. If the theoretical considerations based on the mechanical model is valid for human eyes, corneal pulse amplitudes should be expected to increase with increasing K and decrease with decreasing K . If so, all factors which may influence the size of K (age, refraction, intraocular pressure, hyperemia, congestion, ocular surgery (Draeger 1959, Ytteborg 1961)) may also be expected to influence the size of corneal pulse amplitudes.

It has previously been shown that retinal detachment surgery is followed by a marked decrease in ocular rigidity (Syrdalen 1970b). The present investigation deals with corneal indentation pulse in pre- and postoperative retinal detachment eyes in order to evaluate clinically the possible influence a decrease in K will have upon the corneal indentation pulse amplitudes.

Material

The present investigation took place during Nov. 1968-Aug. 1969. The material consists of patients which at the time of examination were hospitalized or had previously been hospitalized in the eye department Rikshospitalet, Oslo, due to primary retinal detachment in one eye and with a fellow eye without any detachment. No eye is included in which there has been a history of ocular trauma, glaucoma, uveitis or previous ocular surgery (except the actual retinal detachment operation). All patients were examined by the author and all eyes had gonioscopically wide open anterior chamber angles. *Preoperative dynamic tonometry* was performed on 34 patients with an average age of 54.3 years (range from 10 to 79 years). In this group 10 patients (25.6%) were myopic (minus 0.5 or more) and of these 1 (2.6%) exceeded minus 8. *Postoperative dynamic tonometry* was performed on 39 patients with an average age of 52.9 years (range from 10 to 79 years). In this group 12 patients (30.8%) were myopic (minus 0.5 or more) and of these 2 (5.1%) exceeded minus 8. All patients in the postoperative group had been successfully operated for retinal detachment in one eye. 28 of these patients had been operated with encircling procedure (cerclage) either alone or in combination with local silicone rubber full thickness scleral implant(s). 10 of the patients had been operated only with local scleral buckling procedure and one patient had been treated with cryo-

Table I
Ocular rigidity coefficient (K) in fellow eyes and operated detachment eyes in groups in relation to time after operation. N = number of patients in each group
Numbers in brackets = standard deviation of population.

Method of operation	Interval since operation (days)	N	K fellow eyes	K detachment eyes	K fellow - K detach	t value	significance level
Group A Including procedures	9-14 (Average = 11)	3	0.0167 (0.0039)	0.0041 (0.0012)	0.0126	9.974	1 < 0.001
	19-54 (Average = 3)	9	0.0180 (0.0030)	0.0064 (0.0029)	0.0116	7.187	1 < 0.001
	61-100 (Average = 257)	24	0.0200 (0.0041)	0.0063 (0.0018)	0.0137	11.414	1 < 0.001
	Total (Average = 156)	47	0.0189 (0.0046)	0.0059 (0.0017)	0.0130	16.100	1 < 0.001
Group B Local buckling procedures	10-33 (Average = 15)	5	0.0226 (0.0038)	0.0126 (0.0015)	0.0100	5.136	1 < 0.01
	65-100 (Average = 119)	8	0.0185 (0.0035)	0.0161 (0.0039)	0.0024	3.431	1 < 0.02
	Total (Average = 75)	13	0.0201 (0.0012)	0.0147 (0.0036)	0.0054	4.015	1 < 0.005

Method of paired comparison employed by testing the results from fellow eyes against detachment eyes

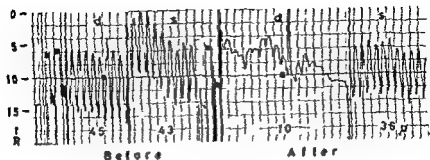


Fig 1

Corneal indentation pulse amplitudes recorded before and after retinal detachment operation (cerclage) right eye d = right eye s = left eye Sensitivity settings 20 mV and μ mV ($2 \text{ mV} = 2 \mu$ per paper division)



Fig 2

Corneal indentation pulse amplitudes recorded before and after retinal detachment operation (local buckling procedure) left eye d = right eye s = left eye Sensitivity settings 20 mV and 2 mV

Comment

Preoperative results In the eyes of the present series corneal indentation pulse amplitudes lower than normal could be expected due to the high incidence of myopia and the possibility of lowered ocular rigidity (Draeger 1959 Castren &

- 2 Carroll J M Martola E L Laibson P P & Dohlman C H Am J Ophth 1967
73 103
- 3 Dawson C Togni B & Moore Jr., T E Arch Ophth 1963 79 p 740
- 4 Dawson C Togni B & Thygeson P Nature 1966 211 p 316
- 5 Epstein M A J Exper Med 1967 115 p 1
- 6 Epstein M A J Cell Biol 196 10 p 539
- 7 Hogan M J Kimura S J & Thygeson P Tr Am Ophth Soc 1963 61 p 75
- 8 Kaufman H E Brown D C & Ellison F D Am J Ophth 1969 60 p 32
- 9 Luria S E & Darnell Jr J E General Virology Wiley & Sons New York London Sydney 1967
- 10 Morgan C Ellison S A Rose H M & Moore D H Proc Soc Exper Biol &
Med 1933 8 p 454
- 11 Morgan C Ellison S A, Rose H M & Moore D H Nature 1934 173 p 209
- 12 Morgan C Ellison S A Rose H M & Moore D H J Exper Med 1934 100
p 19
- 13 Morgan C Rose H M Holden M & Jones E P J Exper Med 1939 110
p 643
- 14 Nilsson S E C Acta Ophth 1969 47 p 947
- 15 Shipkey F H Erlandson R A Bailey R B Babcock V I & Southam C M
Exper Molec Pathol 1961 6 p 39
- 16 Takemura T Exper Eye Res 1963 9 p 303
- 17 Takemura T & Kitano S Acta Soc Ophth Jap 1960 64 p 2979
- 18 Tanaka Y & Kimura S J Arch Ophth 1961 78 p 68
- 19 Watson D H Wildy P & Russell W C Virology 1964 24 p 523
- 20 Wildy P Russell W C & Horne R W Virology 1960 10 p 904
- 21 Wilmer R & Iwamoto T Arch Ophth 1968 89 p 331

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PHOTOCOAGULATION AFTER FANKHAUSER AND LOTMAR

Some clinical experience with a new apparatus

BY

BERTIL LINDER

At the Gonin Club Symposium at Munich in 1966 Fankhauser and Lotmar presented equipment for photocoagulation through the Goldmann three mirror contact glass. One apparatus was connected to the ordinary Zeiss photocoagulator working with a xenon lamp as light source. Another apparatus operated with a quasi continuous ruby laser developed in the Siemens and Halske laboratories by Ross. In 1968 a small series of ten prototypes of a device to be connected to the Zeiss photocoagulator was made in Bern. In Lund we were able to buy one of these devices and since September 1968 it has been in frequent use. In fact since then the photocoagulator has not been used without this device in cases with peripheric lesions. Since no experience with the Fankhauser Lotmar prototype has been presented except in the original articles by the constructors it could be of interest to record our impressions of the device and its use.

As described by Fankhauser and Lotmar the apparatus mounted on a corneal microscope table is connected to the arm of the Zeiss photocoagulator (Figs 1 and 2). The only necessary modification to the photocoagulator is to change the original sieve stop for another delivered with the apparatus. The new sieve stop can also be used in most cases without the Fankhauser Lotmar device (for further explanation see Fankhauser and Lotmar). With the monocular slit lamp the biomicroscopy and consequently the photocoagulation even of the peripheric part of the fundus through the Goldmann three mirror con-

Table I

Corneal indentation pulse amplitudes (μ) pulsесynchronous change in ocular volume (ΔV mm³) and intraocular pressure in mm Hg Schiotz (P_0) recorded in detachment eyes and fellow eyes before operation (N = 34) and after operation (N = 39)

		Detachment eyes		Fellow eyes		t value* sign level	
		Mean	σ	Mean	σ		
Preoperative N = 34	μ	24.41	11.156	24.56	9.633	0.168	—
	ΔV	2.375	0.903	2.378	0.937	1.000	—
	P_0	12.26	4.063	13.04	3.033	1.285	—
Postoperative N = 39	μ	7.28	6.219	20.12	8.522	10.057	$P < 0.001$
	ΔV	0.718	0.597	2.032	0.852	10.093	$P < 0.001$
	P_0	5.75	4.032	14.52	3.124	13.011	$P < 0.001$
Cerclage N = 28	μ	4.14	3.297	20.64	8.469	12.380	$P < 0.001$
	ΔV	0.423	0.339	2.02	0.83	12.301	$P < 0.001$
	P_0	3.8	2.238	14.22	3.423	16.350	$P < 0.001$
Local procedure N = 11	μ	15.27	4.512	20.91	9.071	3.071	$P < 0.02$
	ΔV	1.468	0.429	2.064	0.285	2.995	$P < 0.07$
	P_0	10.7	3.259	15.4	2.221	3.953	$P < 0.001$

* Statistical method of paired comparison

tested using the method of paired comparison. The *preoperative results* show that no difference exists between corneal indentation pulse amplitudes in detachment eyes and fellow eyes. Intraocular pressure is lower in detachment eyes than in fellow eyes, but the difference is not statistically significant. The *postoperative results* yields a marked difference between detachment eyes and fellow eyes. A striking reduction in corneal indentation pulse amplitudes, calculated pulsating ocular volume and intraocular pressure is seen in detachment eyes. This reduction is most pronounced in cerclage operated eyes and more moderate in eyes operated with local buckling procedure. Fig. 1 demonstrates the pre- and postoperative recordings from one of the patients operated with cerclage and Fig. 2 the pre- and postoperative recordings from a patient operated with local buckling procedure.

special value with the instructive drawings of a rather complete series of classical and effective procedures

Before intraocular intervention for cataract glaucoma in cyclectomy and keratoplasty the author strongly recommends pressure reducing massage of the eye which might be brought about by Vorosmarthy's Oculopressor. A rubber pelotte is fixed in front of the eye and insufflated with air. Knowing the preoperative intraocular tension the manometrically controlled pressure to be withheld in the pelotte during ten minutes necessary for reducing the intraocular tension to 0.5 mm Hg can be read from a diagram. The author describes the characteristic effect of this procedure with reduced volume of the vitreous, deepening of the anterior chamber etc.

This book is recommended

P. Brøndstrup

Startup F. G. Diseases of the Canine Eye. Bailhere Tindall & Cassell London 1969
387 pages 272 figures Price £ 6.50

This book is intended primarily for veterinarians who have to treat canine eyes. Here and there however there are interesting subjects in which canine pathology differs essentially from human (pathology of the nictitating membrane, keratitis with pigmentations which interfere with vision, gonioscopy, the motley ophthalmoscopic appearances which make it difficult to recognize abnormalities of the fundus etc.).

A more thorough description of a number of ophthalmomedical subjects is missing, presumably because present knowledge is deficient.

Cataract extraction is described in detail. This procedure may be complicated by adhesions between the lens and vitreous, an increased tendency to fatal haemorrhage from the iris or the ciliary body, capsular rupture and dislocation of the lens. Alpha chymotrypsin is recommended in a higher dosage and for a longer period than is customary in human cases.

The book is well written and has an ample bibliography and index.

M. S. Norn

Therapie der Augenkrankheiten mit diagnostischen Hinweisen. Fibel für Praxis und Klinik. Von Prof. R. Thiel ergänzt von Prof. F. Hollwich. Georg Thieme Stuttgart 1970. XII 527 pp. 17 × 24 cm. Balacron geb. DM 69.

This volume contains an enormous amount of concentrated diagnostics and therapy of ocular affections. In this way it appears most practically valuable for the engaged ophthalmologist. The authors must be highly admired for their ability in precise diagnostic description. In the therapeutical directives one again must be impressed by the gains of the last decades presented up to date, but also by the vast fields where we lack what looks like a specific therapy and are forced to symptomatic and general procedures. In this latter category the book also contains many proposals in some of which the reviewer – partly by education – might find himself of a more nihilistic attitude – well knowing that therapy is at the same time an art and a scientific approach. Sometimes unknown trade marks of drugs cause difficulties.

P. Brøndstrup

mm Hg (local buckling procedure) (Syrdalen 1960b) This hypotony in itself would cause only a minor decrease in corneal indentation pulse amplitudes

Conclusions

- 1 The presence of retinal detachment in an eye will not influence the size of the corneal indentation pulse amplitudes
- 2 In eyes with a low ocular rigidity the corneal indentation pulse amplitudes will show a corresponding decrease
- 3 Dynamic tonometry is not a suitable method to measure intraocular pulse synchronous pressure variations (or volume variations) in eyes where ocular rigidity differs in a major degree from normal such as in operated retinal detachment eyes

Summary

The present investigation reports results of dynamic tonometry in 34 patients with retinal detachment in one eye and with a fellow eye without detachment. Before operation no difference in corneal indentation pulse amplitudes is found between detachment eyes and fellow eyes.

Postoperative dynamic tonometry is performed on 39 patients. In these detachment eyes a marked reduction in corneal indentation pulse amplitudes (and corresponding pulsating volume of the eyes) is seen. The most pronounced reduction is seen in eyes operated with cerclage; a more moderate reduction is seen in eyes operated with local buckling procedure. The postoperative reduction in ocular rigidity in retinal detachment eyes is considered to be the main reason to the decrease in corneal indentation pulse amplitudes seen with the method of dynamic tonometry.

The value of results obtained by dynamic tonometry on paired eyes where ocular rigidity deviates in a major degree from each other is very limited.

References

- Broch A & al. Studies on cerebral and ocular circulation in a patient with cluster headache. *Acta Otolaryng.* 10: 18, 1960.
- Brom A, J. Knox D L & Gaasterland D. Tonographic studies in carotid occlusive disease. *Brit. J. Ophthalm.* 52: 5, 595, 1968.

*Hamburger F A Horror fusionis Bucherei des Augenarztes Vol No 34 F Enke
Stuttgart, 1970 Pp VIII + 66 37 figures Price DM 14 00*

Again Bucherei des Augenarztes has enriched ophthalmology by a useful monograph this time dealing with one of the clinical recesses Horror fusionis Dr Hamburger gives a clear easily comprehensible description and interpretation of the polymorphous complex made up by the different variants of horror fusionis The syndrome of horror fusionis includes according to Hamburger the following elements Persistent diplopia which cannot be corrected by prisms microstrabismus in the form of constant oscillation of the 2 visual axes around zero position apparently normal retinal correspondence abnormal anisophoria, lacking suppression of the image in one eye and repulsion between the image in the right and left eye.

The book comprises not only the syndrome of horror fusionis but also abnormalities of binocular vision from adjoining fields such as physiological horror fusionis disparity of fixation, microstrabismus aniseikonia, etc The book ends in a postscript by Professor A Linksz in which it is stated inter alia that the main problem in horror fusionis appears to be horror suppressionis This monograph may be earnestly recommended to readers who take an interest in the problems of binocular vision

E Gregersen

*Melvin L Rubin and Gordon L Walls Fundamentals of Visual Science Charles C
Thomas Publisher Springfield Illinois U S A 1969 Pp 435 71 illustrations
Price \$ 17 00*

Presenting the fundamental facts about visual sensory processes in a digestible form to clinical ophthalmologists is no easy job Although more than a hundred years have passed since Helmholtz published his *Handbuch der physiologischen Optik* and although Marius Tscherning A V Tschermak Seysenegg Francis Heed Adler and Arthur Linksz among others have made efforts to bring physiological optics back to ophthalmology too few modern ophthalmologists are thoroughly familiar with the mechanisms of contrast sensitivity (as a prerequisite to the understanding of visual acuity) dark adaptation colour vision, depth perception, and so forth Melvin Rubin honours as co author his late friend and mentor Gordon L Walls SCD who died in 1967 as professor of physiological optics at the University of California and whose notes of a lecture course make up the basic material of the book

The aim of the present teaching manual is to stress the inspiring as well as clinically important aspects of visual science and in a very didactic manner the author has succeeded in keeping up the reader's interest

The book is divided into four sections

- (1) Light and basic concepts
- (2) Intensive vision and electrophysiology
- (3) Chromatic vision
- (4) Spatial vision

Of course the author has not devoted himself equally to all the sections Although the first chapter on the physical properties of light may be understood without much previous knowledge of physics the presentation bears too strong traces of American terminology and measuring units to be easy reading to Scandinavians The chapter on visual acuity does not come up to the presentation of the photochemical basis of vision - and especially not up to that of chromatic vision, a topic on which the author has set his heart judging by his previous publications

Pojola 1962) Within certain limits the corneal indentation pulse amplitudes will increase with increasing intraocular pressure and decrease with decreasing intraocular pressure (Horven 1970b) In the present series the average intraocular pressure both in detachment eyes and in fellow eyes is rather low (as previously seen in other series of retinal detachment patients (Sjrdalen 1970a b) At this level of intraocular pressure the recorded corneal indentation pulse amplitudes are close to estimated normal values (Horven 1970b) The small difference in intraocular pressure between detachment eyes and fellow eyes is not expected to induce any larger difference in corneal indentation pulse amplitudes than what demonstrated As there is no significant difference in corneal indentation pulse amplitudes (or corresponding change in intraocular volume) between detachment eyes and fellow eyes the results indicate that the blood supply in detachment eyes is not different from the blood supply in fellow eyes The presence of retinal detachment in an eye does not induce any change in corneal indentation pulse amplitudes This seems logical if one remembers that the main bulk of blood pumped into the eye during systole goes into the choroid

Postoperative results In the total postoperative group corneal indentation pulse amplitudes in fellow eyes were lower than in preoperatively examined fellow eyes This difference is not statistically significant (Student's *t* test $t = 1.792$) and may be caused by difference in materials and the patients getting used to the procedure The postoperative reduction in corneal indentation pulse amplitudes corresponds to postoperative reduction in ocular rigidity previously seen in similar groups of retinal detachment patients (Sjrdalen 1970b) The present study offers therefore clinical evidence of a close relationship between corneal indentation pulse amplitudes and ocular rigidity The smaller the *k* value the smaller corneal indentation pulse amplitudes will be recorded

The ΔV values are calculated by use of converting tables depending on data from eyes with presumably normal ocular rigidity The low postoperative ΔV values listed in table I may therefore be fully explained by the low ocular rigidity in these eyes The actual excess of blood pumped into these eyes during systole may as a consequence be of the same order of magnitude as in the fellow eyes According to earlier theoretical considerations (Sjrdalen 1970b) the cerclage would have to expand only 0.1 mm at each systole in order to increase the ocular volume 2.032 mm³ (postoperative ΔV value of fellow eyes) The pulsating volume of the eye may be the same after operation as before but the method of dynamic tonometry fails in measuring the volume

In the present series intraocular pressure values obtained using Schiotz tonometer and Friedenwald's 1955 table are too low due to the low ocular rigidity The average postoperative intraocular pressure values are therefore quite erroneous Using applanation tonometry the average hypotony of operated detachment eyes compared to fellow eyes was 2.93 mm Hg (cerclage) and 1.92

As a whole the presentation the superb illustrations and the explanatory analogies in the text classify the author as a trained and enthusiastic tutor and as a master of his extensive subject

The book may be recommended to all ophthalmologists as the most up to date and informative book of its kind

V Dreyer

Dallow R L Television Ophthalmoscopy Charles C Thomas Springfield 1970 Pp XII + 104 \$ 8.50

Television ophthalmoscopy means the introduction and application of electronic recording of ocular fundus morphology. It is still a relatively untried system in spite of its initiation in 1950. This is certainly due to advances in fundus photography and cinematography over the same period and a consequent preoccupation with the film medium. Photography is still superior in the fine resolution of details but television ophthalmoscopy – besides being a means of teaching – involves the possibilities of electronic processing and quantitation of fundus data. These parameters are divided into three categories: 1) geometric (static morphologic) data e.g. diameter of the optic disc and the retinal vessels; 2) temporal data e.g. blood circulation time, pulse transmission and retinal artery blood pressure; and 3) chromatic data e.g. evaluation of optic atrophy. The book uncovers a future field of automation that will become of superior importance in fundus studies and necessary too. Should it be possible to present an objective analysis of the diabetic fundus?

P Brandstrup

Schlote W Nervus opticus und experimentelles Trauma. Beitrag zur Cytologie und Cytopathologie eines zentralnervösen Markfasersystems. Monographien aus dem Gesamtgebiete der Neurologie und Psychiatrie Vol 131. Editors M Müller, H Spatz & P Vogel. 156 pages, 61 illustrations (Springer Berlin Heidelberg New York 1970).

The experiments were done on the optic nerve of the rat where the uniform system of nerve fibres offers great advantages. In addition the extracranial course of the optic nerve between the eyeball and the optic canal permits experimental procedures without damage to other parts of the brain.

The author studied the effects of localized trauma of differing intensity to the optic nerve using light and electron microscopy, enzyme and histochemistry from 12 hours to 4 months after the injury. A distinction is made between three different types of posttraumatic sheath breakdown in the optic nerve. The study has been performed with Germanic thoroughness and the illustrations are excellent.

S R. Andersen

Sampson Whitney & Gerald L. Feldman (ed) Contact Lens Medical Seminar Vol I Charles C Thomas Springfield Illinois 1970 169 pg Price \$ 10.50

This is a report of a contact lens seminar held in Palmer House Chicago in connection

JUDICIA DE NOVIS LIBRIS

Unspecific Shock Therapy in Ophthalmology Symposium Ophthalmologicum Warsaw
15-17 October 1969 Travaux de la Société de Sciences et des Lettres de Wrocław
Série B Nr 157 Wrocław Wrocławskie Drukarnia Naukowa. 1969 Pp 253
Price zł 63

The proceedings of the mentioned symposium Part one (19-142) contains the impressive studies of the Warsaw University Eye Clinic of the theoretical and clinical bases of therapy of inflammatory eye diseases with typhoid vaccine and typhoid endotoxin Part two (143-251) consists of papers from other scientific centers dealing with the same subject of nonspecific general stimulation therapy

The classical use and effect of fever therapy are commented by numerous preferably hematologic and serologic studies

In a time with the generally preferred replacement therapy of steroids it is well to recapitulate other effective approaches.

P Brandstrup

Antonin Heine Das verätzte Auge und die Keratoplastik Bucherei des Augenarztes
Heft 52 Ferdinand Enke Stuttgart 1969 91 pages 30 figures 7 tables und 145
references Price DM 20

This book deals with a problem which still awaits its solution The treatment of caustic injuries to the eye The author has given particular attention to lime corrosion and indeed this is reasonable

The introduction is followed by a detailed review of the literature on keratoplasty after caustic injuries The next chapter deals with the treatment and therapeutic results from the Eye Clinic of the Palacky University of Olomouc from the period 1948-1964 comprising a total of 16 eyes The presentation of this material is rather cursory and caustic with many references to previous publications A visual acuity of 5/20 or more was obtained in 21%

The main emphasis is on a series of experiments on lamellar autotransplantation in 47 rabbits As the main conclusion it is stated that a lamellar graft may heal in a cornea with fresh lime corrosion and that the earlier the grafting is done the more favorable is its result On this basis the author advises a chondro-lamellar keratoplasty in cases of human lime corruptions

Niels Ehlers

Jaffe Norman S The Vitreous in Clinical Ophthalmology 310 pages, 334 figures including 11 in colour C V Mosby Comp St. Louis 1969 Price \$ 32.50

The author is assistant professor to the University of Miami School of Medicine and teacher in the Academy of Ophthalmology courses on the vitreous body

The book deals with subjects such as the embryology anatomy ultrastructure, and biochemistry of the vitreous systematic slit lamp examination the ascension phenomenon the condition of the anterior hyaloid membrane after cataract extraction (holes, prolapse vitreous strings) collapse of the vitreous mentioning Linder's thesis the role of the vitreous in retinal detachment in diabetes, in pupillary block, etc.

On A Jensen's studies on primary hyperplastic perivascular vitreous are quoted. The

with the October 1968 meeting of the American Academy of Ophthalm and Otolaryng. Similar seminars are to be held every other year and to be published in the same way. This volume appeared 18 months after the meeting was held.

At the seminar practical aspects were in the foreground. There are chapters on the prescription of contact lens with topogokeratometer on modification and finishing of contact lenses follow up on patients wearing contact lenses wearing time and on special problems such as aphakia keratoconus and postkeratoplasty states on toric lenses on the selection of patients with motor anomalies for contact lenses.

In a chapter on flush fitting lenses as a therapeutic measure in bullous keratitis corrosion, pemphigus etc. it is established that these are highly specialized tasks which should be restricted to hospitals and which require int al a fulltime technician.

The book closes with a report of a lively panel discussion. Great importance is attached to diagnosing incipient corneal oedema as soon as possible i. e. by scleral scatter without magnification.

Reduced or insufficient blinking may give rise to trouble and shorten the wearing time. The anterior surface of the contact lens may be dry. These patients should be instructed in forced blinking e. g. for 10-15 minutes in the event of incipient burning or dimming.

Soft lenses are criticized but possibly have a special indication e. g. instead of flush fitting lenses a matter which may be of interest when Bausch & Lomb's lenses appear on the market.

There are discussions concerning fenestration of minicontact lenses bifocal lenses on front toric back toric and bitoric lenses on dry spots and on Schirmer's test.

The book is readable and worth recommending to all who take an interest in contact lens problems.

M. S. Vorn

- Bynke H G & Krakau C E T A handy instrument for oculo sphygmography with some clinical results *Ophthalmologica* 148 367 373 1964
- Bynke H G & Schele B On the origin of the ocular pressure pulse *Ophthalmologica* 153 29 36 1967
- Bynke H G Influence of intraocular pressure on the amplitude of the corneal pulse. *Acta Ophthal (khh)* 46 1135 1145 1968
- Castren J A & Pojola S Myopia and scleral rigidity *Acta Ophthal (khh)* 40 33 36 1962
- Castren J A & Laavikainen P New method of diagnosing carotid diseases *Acta Ophthal (khh)* 41 219 223 1963
- Davanger M Studier av de pulssynkrona svingninger i øyets trykk Norsk Oftalmologisk Forenings vårmøte May 1963
- Davanger M The ocular pressure and hydrodynamics of the aqueous fluid as illustrated by a mechanical model *Acta Ophthal (khh)* 42 735 752 1964
- Draeger J Untersuchungen über den Rigiditätskoeffizienten *Documenta Ophthal* VIII 431 486 1959
- Flage T & Horven I Corneal indentation pulse in Sturge Weber's syndrome A case report. *Acta Ophthal (khh)* in press 1970
- Horven I Dynamic tonometry I The dynamic tonometer *Acta Ophthal (khh)* 46 1213 1221 1968
- Horven I Dynamic tonometry and choroidal melanoma *Arch Ophthal* 82 440 445 1969
- Horven I Dynamic tonometry II Methods of corneal indentation pulse registration. *Acta Ophthal (khh)* 48 23 37 1970a.
- Horven I Dynamic tonometry III The corneal indentation pulse in normal and glaucomatous eyes *Acta Ophthal (khh)* 48 39 57 1970b
- Horven I Dynamic tonometry IV The corneal indentation pulse in giant cell arteritis *Acta Ophthal (khh)* in press 1970c
- Horven I & Syrdalen P Corneal indentation pulse and general anesthesia *Acta Ophthal (khh)* 48 59-66 1970
- Syrdalen P & Horven I Corneal indentation pulse and retrobulbar anesthesia *Acta Ophthal (khh)* 48 59 66 1970
- Syrdalen P Intraocular pressure and ocular rigidity in patients with retinal detachment I Preoperative study *Acta Ophthal (khh)* in press 1970a
- Syrdalen, P Intraocular pressure and ocular rigidity in patients with retinal detachment II Postoperative study *Acta Ophthal (khh)* in press 1970b
- Suuki I Corneal pulsation and corneal pulse wave *Jap J Ophthal* 6 190 194 1962
- Weber K Inaug Diss Marburg 1850 cited by Wegener W. Neue Ergebnisse über die pulsatorischen Schwankungen des menschlichen Bulbus und seiner Hüllen *Arch f Augenheilk* 102 1 21 1930
- Ytteborg J The role of intraocular blood volume in rigidity measurements on human eyes *Acta Ophthal (khh)* 38 410 436 1960
- Ytteborg J On scleral rigidity Oslo University Press Forum Boktrykkeri Oslo 1961

VARIA

European Ophthalmic Pathology Society

Held its ninth annual meeting in Ghent Belgium from 28th 30th May 1970 Dr F C Blodi (Iowa City U S A) and Professor J François (Ghent) were the guests of honour Invited guests were Dr E Balestrazzi (Italy) and Prof M Brihaye van Geertruyden (Belgium) The meeting was attended by 31 members The next meeting will be a Joint Meeting with the American Verhoeff Society which is celebrating its 25th anniversary and will be held in London on the 25th to 28th April 1971 Prof N Ashton will act as organising secretary

The XX Nordic Ophthalmological meeting

will be held in Reykjavik on June 23rd to 26th 1971

- 1 The intraocular pressure
- 2 Diabetes mellitus and the Eye

There will be an opportunity to read papers other than those on the main subjects Further informations concerning announcements hotelbookings etc. will be given out at a later date

Any inquires can be directed to Augnlæknafélag Islands (Icelandic Ophthalmological Society) box 954 Reykjavik

increase of cornea and lenticular power and possibly also an unrelated decrease of axial length occurs in young people after the age of 14 Sex differences were not obvious and bodily length and weight without relationship

Our knowledge of dynamics of the infantile eye below 3 years of life = still poor
The concept of Emmetropization is considered outmoded

P Brändstrup

Recent Research on the Retina British Medical Bulletin vol 26 No 2 Brit Council
London, May 19 0

Our readers attention are drawn to this volume of British Medical Bulletin. Prof N Ashton acted as Chairman of the committee that planned this number and Prof E S Perkins as scientific editor The volume contains 17 chapters on recent advances in retinal research Most of the work are British and the authors of high esteem
H Ehlers

Keeney Arthur H (editor) *Proceedings of the Eleventh Annual Meeting of the American Association for Automotive Medicine* C. C. Thomas Springfield Illinois
19 0 '93 pages including index and illustrations Price \$ 19 15

Traffic accidents and traffic medicine are gaining ever increasing importance in industrialized society This has int. al given rise to the foundation of The American Association for Automotive Medicine which has now existed for 10 years and on this occasion has published the present monograph

The book comprises 93 chapters dealing with widely different subjects related to traffic injuries and traffic safety (alcohol, analysis of accident materials, psychological factors, driving research) medical aspects in driver licensing attacks of d. ea. e with loss of consciousness during driving prophylactic measures such as teaching propaganda and safety helmets etc)

Chapters of more specific ophthalmological interest are e. g. Drug induced Disturbances of Vision that May Affect Driving (W. Morton Grant) Ocular Findings in Extension Flexion Injuries of the Cervical Spine (William J. Gibson) and Some Relationships between Vision and Driving (Albert Burg) In this last mentioned chapter emphasis is laid on the requirement for developing a cheap and compact apparatus for testing dynamic vision and a well suited equipment for testing night vision (threshold and glare recovery measurements)

The book may be recommended to the ever increasing number of doctors and other specialists who are being involved in the different aspects of traffic medicine.

E Gregersen

Slafovics Kessler E *nggriffe am* Aug. 4 edit. by D Vorosmarthy Enke Stuttgart
19 0 VII 49C pp 5 1 figs DM 107

The three former editions of this ocular surgery appeared in 1933 1945 and 1959 This fourth edition has been thoroughly revised by Vorosmarthy but its general character of a handy precise, well selected presentation has remained.

The chapter dealing with surgery of the eyelids (115 pages) has always been of

*(From the Ophthalmological Department
Central Hospital Nausted (Head Viggo Clemmensen M D)
and The Umanaq Health Service (Medical Officer P H Alsbrk)*

PRIMARY GLAUCOMA IN GREENLAND (Umanaq District)

I Introduction The Normal Intraocular Pressure

BY

P H ALSBRK

The epidemiology of the main types of glaucoma is being studied in many countries during the present years. Complete understanding of the genetic and other etiologic factors on which it depends is slowly approaching. The two major types of primary glaucoma are open angle glaucoma (o a g) and angle closure glaucoma (a c g). The former disease is a prominent cause of blindness in Europe, America and Africa, where it occurs more frequently than angle closure glaucoma. Among the Mongoloids of Asia glaucoma seems to be infrequent; our scattered knowledge within this field suggests, however, that angle closure glaucoma is the more frequent of the two forms. This appears, for instance, from studies made in Burma (a c g/o a g rate 330/25) and in Thailand and among Chinese from Hong Kong and Singapore (Ida Mann 1966, Loh 1968). Mann's geographic studies suggest, as does clinical experience, that the two types of glaucoma are separate disease entities depending in particular on genetic factors which seem to be unequally distributed throughout the world. However, systematic surveys of populations outside Europe and the U S A which might further illustrate the *alloba* pattern would be highly desirable.

The arctic zones of the earth are inhabited by small groups of people who through innumerable generations have lived in total or relative isolation – and

Received October 29th 1969

classification into cases occurring at an early stage of gestation and entailing multiple defects (microphthalmos iridic coloboma glaucoma retinal dysplasia) as distinguished from late cases which are uncomplicated ■ emphasized as being of great value

Bleeding into the various sites and spaces of the vitreous ■ mentioned and the prognosis of the various forms of bleeding is tentatively set up

Central effusion in the macular area and vitreous traction in the posterior pole inherited diseases of the vitreous (Wagner's degeneration (defect in the primordium of the secondary vitreous body Goldman Favre's degeneration and hereditary juvenile retinoschisis) are discussed

Amyloidosis is reviewed general as well as localized in the vitreous The few but interesting attempts at exchanging the vitreous are reported

Under the heading of vitreous surgery the author also mentions the very advanced technique of cutting membranes and deep adhesions as well as vitreous transfer and vitreous replacement

He emphasizes the role of the vitreous body in cataract extraction If loss of vitreous has occurred he recommends bending the cornea and removing all the vitreous tissue remaining in the anterior chamber by means of cellulose sponges so that the iris retracts and the vitreous is left at or behind the pupillary level

In postoperative corneal oedema caused by vitreous strings which do not yield to pupillary dilatation and osmotic treatment the author recommends removal of all vitreous tissue from the anterior chamber This is done by sclerotomy and an open sky procedure using the above mentioned cellulose sponges

To reduce the volume of the vitreous body during cataract extraction the author administers glycerol 90 g by mouth 90 minutes prior to the operation This shrinks the vitreous and reduces the risk of loss or prolapse of the vitreous body No major side effects are said to have occurred in the author's 1500 cases

This book affords an admirable didactic presentation of the subject with a clear classification good illustrations and up to date references It may be recommended as an excellent modern description of problems relating to the vitreous body

M S Norn

Sorsby, A & G A Leary A longitudinal study of refraction and its components during growth Medical Research Council S R S 309 London Her Majesty's Stationary Office 1970 Pp 41 Price 9s 0d (45p) net

The present study should be read as a supplement to the Council's series No 301 and 293 Professor Sorsby and his colleagues in a cross sectional study of 1400 children between the ages of 3 and 15 presented the evidence that the optical components of the eye do not vary freely but are correlated so that high powers of the cornea and lens go with short axes and low powers with long axes A considerable range of axial length may be accompanied by emmetropia provided complete correlation Incomplete correlation accounts for all spherical errors except high hypermetropia and high myopia usually determined by axial length

In the actual study 129 of the original children were further followed up The rapid growth of the infantile eye is followed by a gradual slowing until puberty In 75% axis length increase 1 to 1.5 mm considered normal while in 25% ■ higher anomalous increase ■ seen Anomalous elongation ■ not counteracted by a corresponding reduction of cornea and lenticular power and plays a considerable role in reduction of high hypermetropia and development of myopia It has been observed that paradoxical

under conditions as regards light and temperature which differ greatly from the physical environments of the more densely populated parts of the earth

In northern parts of the USSR glaucoma is the most frequent cause of blindness (in 35 per cent of the blind) The cases are often severe with a painful course The number of persons consulting doctors increase greatly during the dark and cold period of the year Acute glaucoma accounts for about 19 per cent of the cases (*Balyasnikova* 1963) No mention is made of gonioscopic findings

In Iceland glaucoma is the cause of blindness in 60 per cent of the blind who in 1950 were 3 per thousand of the population (*Bjornsson* 1967) Through a 25 year period *Sveinsson* (1959) examined 1544 glaucoma patients of whom 90 per cent suffered from glaucoma simplex and less than 2 per cent from acute glaucoma Two thirds of the patients were men Predisposition to glaucoma and/or blindness was found in almost half of the cases Among 237 patients with primary glaucoma *Bjornsson* found by gonioscopy 6 per cent with angle closure glaucoma and only 2.1 per cent who had shown actual attacks

As regards the *Esimo* populations our knowledge is limited According to *Ida Mann* glaucoma is rare most frequently of the narrow angle type as among the Mongoloids In 1968 *Speakman* found among 200 adult Eskimos in Canada three with angle closure glaucoma and two with pronounced chronic glaucoma

Earlier observations with regard to glaucoma in *Greenland* was summarized by *Bertelsen* in his large nosography (1940a) Primary glaucoma has been mentioned as early as 1909 and is said to occur relatively frequently both in northern and southern districts and to be an important cause of blindness (*Norman-Hansen* 1911 *Borresen* 1926 *Hertz* 1929 *Skeller* 1949)

Blindness is much more frequent in *Greenland* than in other parts of Denmark in 1937 it was thus ten times as frequent in the population groups above 16 years of age During the years 1910-1929 the frequency of blindness was 3 per thousand with leucomas and glaucoma as the most frequent causes (*Bertelsen* 1940b) In 1962 the ophthalmologists *Clemmesen* and *Skydsgaard* studied the prevalence of blindness on *Greenland's* west coast and found it to be 2.5 per thousand (*Skydsgaard* 1963) Among 69 blind persons 44 were blind from primary or secondary glaucoma 39 of them with vision of 1/60 or less Of those who were blind due to glaucoma almost 80 per cent were women In the latest statistics - from 1968 - the prevalence of blindness was found to be 3 per thousand (*Clemmesen* 1969)

By way of comparison mention may be made of the latest survey made in Denmark and comprising the island of *Falster* It is based on the same blindness criteria (visual acuity $\leq 4/60$) and covers a population slightly larger than that of *Greenland* Here *Narshov* (1968) found a blindness prevalence of 1.24 per thousand likewise with primary glaucoma as the most frequent cause (in 29

Again *Bucherei des Augenarztes* has enriched ophthalmology by a useful monograph, this time dealing with one of the clinical recesses *Horror fusionis*. Dr Hamburger gives a clear easily comprehensible description and interpretation of the polymorphous complex made up by the different variants of *horror fusionis*. The syndrome of *horror fusionis* includes according to Hamburger the following elements: Persistent diplopia which cannot be corrected by prisms; microstrabismus in the form of constant oscillation of the 2 visual axes around zero position; apparently normal retinal correspondence; abnormal anisophoria, lacking suppression of the image in one eye and repulsion between the image in the right and left eye.

The book comprises not only the syndrome of *horror fusionis* but also abnormalities of binocular vision from adjoining fields such as physiological *horror fusionis*, disparity of fixation, microstrabismus, aniseikonia etc. The book ends in a postscript by Professor A. Linksz in which it is stated int. al. that the main problem in *horror fusionis* appears to be *horror suppressionis*. This monograph may be earnestly recommended to readers who take an interest in the problems of binocular vision.

■ Gregersen

Melvin L. Rubin and Gordon L. Walls: Fundamentals of Visual Science Charles C Thomas Publisher Springfield Illinois U S A 1969 Pp 435 71 illustrations
Price \$ 17.50

Presenting the fundamental facts about visual sensory processes in a digestible form to clinical ophthalmologists is no easy job. Although more than a hundred years have passed since Helmholtz published his *Handbuch der physiologischen Optik* and although Marius Tscherning, A. V. Tschermak, Seysenegg, Francis Heed Adler and Arthur Linksz among others have made efforts to bring physiological optics back to ophthalmology, too few modern ophthalmologists are thoroughly familiar with the mechanisms of contrast sensitivity (as a prerequisite to the understanding of visual acuity), dark adaptation, colour vision, depth perception, and so forth. Melvin Rubin honours as co-author his late friend and mentor Gordon L. Walls, M.D., who died in 1962 as professor of physiological optics at the University of California and whose notes of a lecture course make up the basic material of the book.

The aim of the present teaching manual is to stress the inspiring as well as clinically important aspects of visual science and in a very didactic manner the author has succeeded in keeping up the reader's interest.

The book is divided into four sections:

- (1) Light and basic concepts
- (2) Intensive vision and electrophysiology
- (3) Chromatic vision
- (4) Spatial vision

Of course the author has not devoted himself equally to all the sections. Although the first chapter on the physical properties of light may be understood without much previous knowledge of physics, the presentation bears too strong traces of American terminology and measuring units to be easy reading to Scandinavians. The chapter on visual acuity is not concerned with the presentation of the photochemical basis of vision and especially not with that of chromatic vision, a topic on which the author has set his heart, judging by his previous publications.

per cent) As regards the whole of Denmark the blindness prevalence is generally stated to be 0.75-1 per thousand

The part played by glaucomatous diseases in the great problem of blindness in Greenland is thus of such significance as to motivate a more intensive study of a larger group of the population. The main object of such a population study would be to throw light upon the prevalence and types of glaucomatous diseases in the district. However, fundamental epidemiological knowledge within this field might serve as a valuable basis for intensified diagnostic, therapeutic and prophylactic efforts throughout the whole of Greenland and probably have more general significance.

Glaucoma Survey in the Umanaq District in 1967

1) Geography, Population and Health Service

Umanaq district is situated on the west coast of Greenland in about 71° northern latitude, the same latitude as the North Cape of Norway. In this district the dark period of the year lasts from the beginning of November to the beginning of February, and during a corresponding period of the summer the sun does not set. The population is Eskimoic with a certain admixture of Caucasian blood. On December 31, 1966 it numbered altogether 2289 persons. The main town of the district, Umanaq, which is situated on a small island, has a population of 934, of which 844 are Greenlanders. The remaining population in the district - 1345 Greenlanders and 10 non Greenlanders - lives in eight villages at distances of from 21 to 123 kilometres from the town. Medical service is provided by two doctors, two to three nurses and a midwife who are stationed in the town, but who are on frequent tours or called out to the villages whenever the sea is navigable or the ice safe for dog sledge transport. During several weeks annually - before and after the sledge season - it is impossible for people living in the villages to consult a doctor. Each village is attended by a native, part-trained midwife who has been given an education including nursing and first aid for three to four years at a local hospital. However, her theoretical knowledge - also with regard to eye diseases - is very limited. She has a comprehensive store of medical agents comprising medications for the management of glaucoma. Wireless connection from the villages to the town was established as late as 1968. Different ophthalmologists visit the district every or every second year for a few days, but the time at their disposal is sufficient only for superficial examinations, and the standard equipment available does not allow for the performance of biomicroscopy, gonioscopy or applanation tonometry. For the remaining part of the year, ophthalmological problems must be looked after to the best of their ability by doctors without

special value with the instructive drawings of a rather complete series of classical and effective procedures

Before intraocular intervention for cataract glaucoma in cyclectomy and keratoplasty the author strongly recommends pressure reducing massage of the eye which might be brought about by Vorosmarthy's Oculopressor. A rubber pelotte is fixed in front of the eye and insufflated with air. Knowing the preoperative intraocular tension the manometrically controlled pressure to be withheld in the pelotte during ten minutes necessary for reducing the intraocular tension to 0.5 mm Hg can be read from a diagram. The author describes the characteristic effect of this procedure with reduced volume of the vitreous deepening of the anterior chamber etc.

This book is recommended

P Brandstrup

Startup F G Diseases of the Canine Eye Bailliere Tindall & Cassell London 1969
387 pages 272 figures Price £ 6.50

This book is intended primarily for veterinarians who have to treat canine eyes. Here and there however there are interesting subjects in which canine pathology differs essentially from human (pathology of the nictitating membrane, keratitis with pigmentations which interfere with vision, gonioscopy, the motley ophthalmoscopic appearances which make it difficult to recognize abnormalities of the fundus etc.).

A more thorough description of a number of ophthalmomedical subjects is missing, presumably because present knowledge is deficient.

Cataract extraction is described in detail. This procedure may be complicated by adhesions between the lens and vitreous, an increased tendency to fatal haemorrhage from the iris or the ciliary body, capsular rupture and dislocation of the lens. Alpha-chymotrypsin is recommended in a higher dosage and for a longer period than is customary in human cases.

The book is well written and has an ample bibliography and index.

M S Norn

Therapie der Augenkrankheiten mit diagnostischen Hinweisen Fibel für Praxis und Klinik Von Prof. R. Thiel, ergänzt von Prof. F. Hollwich Georg Thieme Stuttgart 1970 XII 527 pp. 17 × 24 cm Balacron geb. DM 69

This volume contains an enormous amount of concentrated diagnostics and therapy of ocular affections. In this way it appears most practically valuable for the engaged ophthalmologist. The authors must be highly admired for their ability in precise diagnostic description. In the therapeutical directives one again must be impressed by the gains of the last decades presented up to date, but also by the vast fields where we lack what looks like a specific therapy and are forced to symptomatic and general procedures. In this latter category the book also contains many proposals in some of which the reviewer – partly by education – might find himself of a more nihilistic attitude – well knowing that therapy is at the same time an art and a scientific approach. Sometimes unknown trade marks of drugs cause difficulties.

P Brandstrup

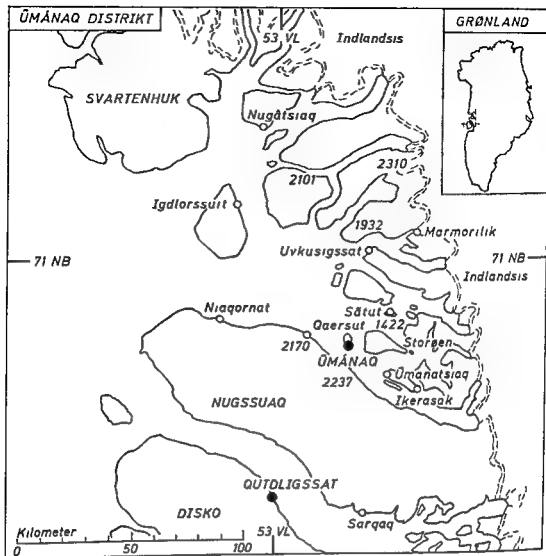


Fig 1
(Map of Umanaq district)

The complex of islands peninsulas and ice fiords of the Umanaq bay. The town and the eight villages are scattered over an area of about the same magnitude as Kattégat. The neighbouring districts are to the north Upernavik and to the south Qutdligssat and Jakobshavn.

ophthalmological training. *Alsbirk & Schioler* (1969) have given a description of the medical work and the morbidity in the district.

2) Preliminary Glaucoma Occurrences

During the period 1964-1966 nine attacks of intermittent and acute glaucoma

Again Bucherei des Augenarztes has enriched ophthalmology by a useful monograph this time dealing with one of the clinical recesses Horror fusionis Dr Hamburger gives a clear easily comprehensible description and interpretation of the polymorphous complex made up by the different variants of horror fusionis The syndrome of horror fusionis includes according to Hamburger the following elements Persistent diplopia which cannot be corrected by prisms microstrabismus in the form of constant oscillation of the 2 visual axes around zero position, apparently normal retinal correspondence abnormal anisophoria, lacking suppression of the image in one eye and repulsion between the image in the right and left eye

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E Gregersen

*Melvin L Rubin and Gordon L Walls Fundamentals of Visual Science Charles C. Thomas Publisher Springfield Illinois U S A 1969 Pp 435 71 illustrations
Price \$ 11 00*

Presenting the fundamental facts about visual sensory processes in a digestible form to clinical ophthalmologists is no easy job Although more than a hundred years have passed since Helmholtz published his *Handbuch der physiologischen Optik* and although Marius Tscherning A V Tschernak Seysenegg Francis Heed Adler and Arthur Linkaz among others have made efforts to bring physiological optics back to ophthalmology too few modern ophthalmologists are thoroughly familiar with the mechanisms of contrast sensitivity (as a prerequisite to the understanding of visual acuity) dark adaptation colour vision, depth perception and so forth Melvin Rubin honours as co author his late friend and mentor Gordon L Walls M.D. who died in 1966 as professor of physiological optics at the University of California and whose notes of a lecture course make up the basic material of the book

The aim of the present teaching manual is to stress the inspiring as well as clinically important aspects of visual science and in a very didactic manner the author has succeeded in keeping up the reader's interest

The book is divided into four sections

- (1) Light and basic concepts
- (2) Intensive vision and electrophysiology
- (3) Chromatic vision
- (4) Spatial vision

Of course the author has not devoted himself equally to all the sections Although the first chapter on the physical properties of light may be understood without much previous knowledge of physics the presentation bears too strong traces of American terminology and measuring units to be easy reading to Scandinavians The chapter on visual acuity does not come up to the presentation of the photochemical basis of vision – and especially not up to that of chromatic vision a topic on which the author has set his heart, judging by his previous publications.

were detected and treated. The patients were seven women from 46 to 63 years of age without any earlier history of glaucoma. Two of the cases were so severe that vision was lost on the eye in question; the others were successfully controlled by medical treatment. One man with poor vision and three women who on account of glaucoma attacks were without perception of light died during this period. From before 1964 another two cases were known of women without perception of light in one and both eyes respectively due to typical glaucoma attacks.

This accumulation of glaucoma attacks in such a small population comprising just under 200 women above the age of forty was the direct inspiration and basis of the present study.

3) Method

Systematic glaucoma surveys of larger groups of the population in Greenland have not been published previously and the available papers do not enable any classification of the glaucoma cases according to gonioscopic findings. As mentioned clinical experience suggested a considerable incidence of angle closure glaucoma in Umanaq district.

It could hardly be expected that it would be possible by tonometric methods to detect a c.g. cases in the interparoxysmal periods. It was nevertheless decided primarily to perform a tonometric screening in order to determine the tension level of normal eyes, the extent to which ocular hypertension occurs and to detect unknown cases of o.a. and advanced cases of a.c.g. Secondly it was planned to extend the examination programme to comprise methods which were more adequate for the detection of a.c. cases also at earlier stages.

Tonometric anamnestic screening was therefore performed as follows: the national register for the district was gone through systematically and punch cards written out for all Greenlanders who on January 31, 1966 had attained the age of twenty in the town and forty in the villages. The register had just been carried up to date with this date as terminal date.

People were invited to attend the examination by a letter in Greenlandic in which a brief description of the object of the examination and of the procedure was given. In the town the examination took place in a ward in the hospital and in the villages in the school room. Two beds or two couches consisting of decks with rugs were placed with the heads immediately below a red disk in the ceiling. Each person was present during the examination of his predecessor to reassure and to make the procedure clear. Persons to be examined were made to rest on the couch for exactly five minutes to calm down before tonometry was performed. All examinations were made by the author assisted by an interpreter and in most cases by a nurse.

The following observations were made in the order named

Front view of the Fankhauser Holmar device connected to the Zeiss photocapagulator

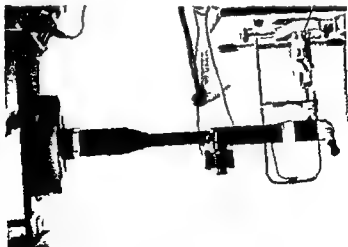


Fig 1



Fig. 2
Side view

*From the University Eye Clinic Lund Sweden
(Head Professor Erik Palm M D)*

PHOTOCOAGULATION AFTER FANKHAUSER AND LOTMAR

Some clinical experience with a new apparatus

BY

BERTIL LINDER

At the Gonin Club Symposium at Munich in 1966 Fankhauser and Lotmar presented equipment for photocoagulation through the Goldmann three mirror contact glass. One apparatus was connected to the ordinary Zeiss photocoagulator, working with a xenon lamp as light source. Another apparatus operated with a quasi continuous ruby laser developed in the Siemens and Halske laboratories by Ross. In 1968 a small series of ten prototypes of a device to be connected to the Zeiss photocoagulator was made in Bern. In Lund we were able to buy one of these devices and since September 1968 it has been in frequent use. In fact since then the photocoagulator has not been used without this device in cases with peripheric lesions. Since no experience with the Fankhauser Lotmar prototype has been presented except in the original articles by the constructors it could be of interest to record our impressions of the device and its use.

As described by Fankhauser and Lotmar the apparatus mounted on a corneal microscope table is connected to the arm of the Zeiss photocoagulator (Figs 1 and 2). The only necessary modification to the photocoagulator is to change the original sieve stop for another delivered with the apparatus. The new sieve stop can also be used in most cases without the Fankhauser Lotmar device (for further explanation see Fankhauser and Lotmar). With the monocular slit lamp the biomicroscopy and consequently the photocoagulation even of the peripheric part of the fundus through the Goldmann three mirror con-

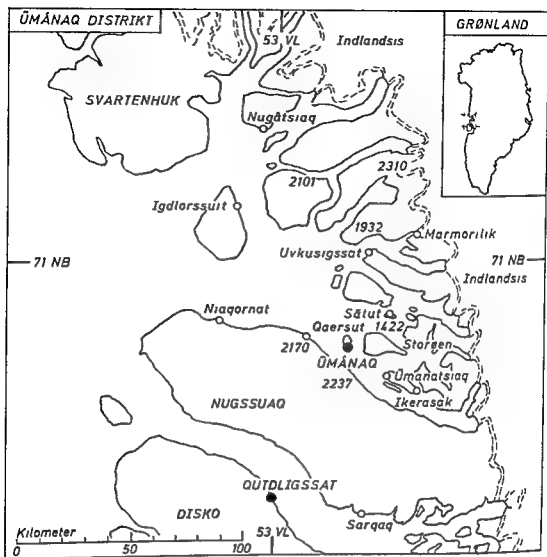


Fig 1
(Map of Umanaq district)

The complex of islands peninsulas and ice fiords of the Umanaq bay. The town and the eight villages are scattered over an area of about the same magnitude as Kattegat. The neighbouring districts are to the north Upernavik and to the south Qutdligssat and Jakobshavn.

ophthalmological training. *Alsbræk & Schioler* (1969) have given a description of the medical work and the morbidity in the district.

2) Preliminary Glaucoma Occurrences

During the period 1964-1966 nine attacks of intermittent and acute glaucoma

very little in comparisons of the results from town and villages with respect to the age group above forty

The fact that the town population was examined between 16 and 18 o'clock and the villagers at different times does however tend to diminish the possibility of ascertaining any possible small differences because due to physiological diurnal variations in the intraocular pressure the highest values will obtain in the morning and the lowest in the evening (*Kataavisto* 1964)

The mean tension of the normal eye in Greenlanders has thus been found to be 15.7 mm Hg (corresponding to a scale reading of 8 with 7.5 g weight on the Schiøtz tonometer) and a standard deviation of 3.0 mm Hg

Discussion

For epidemiological surveys of the prevalence of glaucoma and the normal ocular tension in large population groups Schiøtz tonometry has been used extensively until recently. Table III lists the results of a number of such surveys which compared to the findings from Umanaq district show that normal eyes in Greenlanders do not on the whole differ from American German Finnish Norwegian or British eyes. *Leydhecker et al* (1958) found no difference between right and left eyes or sexes while *Kataavisto & Sammalqvist* (1964) and *Hollows & Graham* (1965) found significantly higher tensions in women than in men -

Table III
Schiøtz tonometry applied to normal eyes
(according to Friedenwald's calibration 1955)

	Number of eyes	Mean tension mm Hg	Standard dev mm Hg
Becker 1958	909	16.1	2.80
Leydhecker et al 1958	19 880	15.5	2.57
Kataavisto & Sammalqvist 1963	11 520	16.00	2.72
Bertelsen T et al 1965	3812	14.8	2.7
Hollows & Graham 1965			
men left eye Schiøtz	1914	14.6	2.96
men left eye applanation	1873	(15.9)	(2.87)
women left eye Schiøtz	2258	15.7	2.87
women left eye applanation	2169	(16.6)	(2.88)
Alsbirk 1967	1108	15.7	3.0

examined in bright daylight – to maintain the same examination times in town and villages was impossible for practical reasons

4) Material

The population groups examined comprised as mentioned all Greenlanders in the town of Umanaq who had attained twenty years of age and all in the villages who had attained the age of forty

Table I gives the distribution of the subjects according to age sex and place of residence the sex distribution is almost equal Fig 2 shows how relatively young the population is The age group 20-39 amounts to 23.9 per cent of the population – almost as in the rest of Denmark – but in Umanaq district there are only 18.5 per cent who are more than forty years of age – as against 41.5 per cent in the rest of Denmark On the whole the age distribution is the same as in the whole of Greenland

Before the completion of the survey there was a small diminution in numbers due to deaths and removals to other districts There were six inhabitants in the district whom we did not succeed in getting hold of because they were away fishing or working in the mines or were not interested in cooperation Only one – an old paranoid psychotic woman – refused categorically to be examined

Table I
Person examined in Umanaq district 1967

Age	Town		Villages		Whole district		Total ♂ + ♀
	♂	♀	♂	♀	♂	♀	
0-9	39	47	—	—	39	47	86
10-19	41	61	—	—	41	61	102
20-39	80	108	—	—	80	108	188
40-49	32	17	41	47	73	64	137
50-59	21	29	49	33	70	64	134
60-69	12	16	35	34	47	50	97
70-79	5	5	7	5	12	10	22
80+	1	1	1	3	2	4	6
40-80+	71	63	133	174	204	197	396
0-80+	151	166	133	174	284	300	584

in the Finnish survey particularly in the age groups 50-59 and 60-69 years. In the latter study a significant difference was also observed between right and left eyes with a slightly higher tension in left eyes.

Results obtained by means of Goldmann's applanation tonometer are more reliable and better comparable than those from a weight tonometer as the Schiotz tonometer. Comprehensive analyses of the influence of age and sex using applanation tonometry have confirmed that in the age group above forty the intraocular pressure is higher in women than in men (Armaly 1965, Hollows & Graham) and further that it increases with age most markedly in women (Armaly). The latter author considers the results to be related to the hormonal changes of the menopause. He found moreover the standard deviations to increase significantly with age equally much in both sexes.

Since Leydhecker's tonometric screening of 10 000 persons deviations from the Gaussian curve on high tension levels have played a great part in glaucoma discussions. Leydhecker *et al.* (1958) showed the distribution to consist of a minor partial collective in the high tension range - in his view representing incipient pathological cases - and a major main collective accurately accounted for by the Gaussian distribution curve.

The sharp assessment of suspect and definitely pathological tension values at $\bar{x} + 2s$ and $\bar{x} + 3s$ respectively has been strongly criticized however and the discussion is still going on. Compare for instance the Tutzing Castle Symposium 1966 and Pollack (1968).

Davanger (1965) considers persons with both intraocular hypertension and simple glaucoma to represent purely quantitative extremes in the high tension range consequent upon the physiological increasing resistance in the porous system of the trabecular meshwork which occurs with age. With normal distribution of effective pore diameters in the population it will be seen by applying simple flow physiological laws to the problem that the same constriction of the pores for instance 5 per cent will result in a higher increase in tension on a high pressure level than on a low pressure level. According to Davanger the skewness to the right is thus an expression of an actual deviation from the Gaussian distribution secondary to the normally distributed pore diameters.

According to Armaly's and Hollows & Graham's thorough surveys of representative samples the distribution is still skew to the right with preponderance on the high tension levels but it has also been shown that viewed separately within the individual age and sex groups the distribution seems normal. It is only when the age is above sixty that a significant preponderance of high values will be found.

The population group with which the present study is concerned is too small to allow such detailed analyses. There is however no marked skewness to the right in the curves of fig. 4. Even when the values for both sexes and both eyes are combined in one curve (fig. 5) the conclusion must be that this material does

a) Classification of the *physiognomy* of the person examined as being "Esquimaux" or "mixed" when judged at a distance before the colour of the eyes could be seen

b) Observation of the *colour of the iris* which was recorded as being either "pure brown" or "mixed"

c) Recording of such abnormalities in the *anterior segment* of the eye as were immediately visible in strong light (diseases of the cornea or iris or their sequelae besides obvious cases of cataract)

d) Determination of the *intraocular pressure* (right eye first) by means of a *tension indicator according to the applanation principle* designed by Bruun Jensen (1967) after anaesthesia and staining of the tear fluid with fluorescein. The tension was determined as being above equal to, or lower than 21 mm Hg

e) Measurement of the *intraocular pressure* with a *Schiotz tonometer* (Riester No 4920) adjusted and controlled on Sept 18 1966 at the Danish tonometer centre and found by micrometric control to be in order after the completion of the screening. A 7.5 g weight was applied and the mean value of the first few oscillations expressed to the nearest whole or half scale unit was recorded. For one day's measurements in one of the villages it became necessary to use another Schiotz tonometer but subsequent micrometric control showed this instrument to be correct and in full agreement with the former one.

As regards relations between scale units and intraocular pressures in mm Hg Friedenwald's calibration (1955) was used.

f) When the measurements were completed the person was asked whether there were *blind persons in his family* either among parents grandparents or other relatives.

g) The person examined was interviewed as to *previous serious eye diseases*. Only information which was relevant in connection with items c) d) and e) was recorded however.

h) The person was asked whether *ophthalmological examination had been performed previously* (all ophthalmological case records were subsequently studied with a special view to previous tension determinations).

i) By means of a flash light and a *halo-meter* (from Campbell Pharmaceuticals Inc.) rainbow rings around a source of light were demonstrated. The interviewer asked the following question uniformly of everybody: "Have you seen such coloured rings round light when you have suffered from a headache?" On an affirmative reply more detailed data with regard to such cases were recorded.

On account of transport problems and for other reasons the people in the town were all examined during the months of January February and the beginning of March and the inhabitants of the villages during May June and July. The people living in the town were thus all examined during the afternoon darkness (from 16 to 18 o'clock) while those in the villages were always

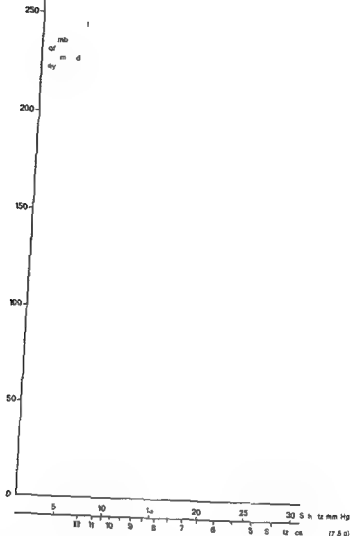


Fig 5

Intraocular pressure of normal eyes Distribution curve for 1108 eyes without reference to right or left eyes or sex. The curve has a smooth course through whole and half tonometer scale units and illustrates the absence of skewness to the right.

not show any skewness to the right on high tension levels. It should be pointed out, however, that 78.6 per cent of the persons examined were under sixty years of age.

Correct sampling of the subjects to be used for studies of normal physiological conditions as the intraocular pressure is of fundamental importance. Healthy people in their usual environments are better probands than for instance patients in non ophthalmological departments — who have frequently been used (example Katavisto & Sammalkivi). The Umanaq survey is a total population study as regards the age groups above forty and in the case of the town popu

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Before the completion of the survey there was a small diminution in numbers due to deaths and removals to other districts. There were six inhabitants in the district whom we did not succeed in getting hold of because they were away fishing or working in the mines or were not interested in cooperation. Only one – an old paranoid psychotic woman – refused categorically to be examined.

Table I
Persons examined in Umanaq district 1967

Age	Town		Villages		Whole district		Total ♂ + ♀
	♂	♀	♂	♀	♂	♀	
0–19	88	47	—	—	39	47	86
20–39	41	61	—	—	41	61	102
40–49	50	108	—	—	80	108	188
50–59	32	17	41	47	73	64	137
60–69	21	29	49	35	70	64	134
70–79	12	16	35	34	47	50	97
80–89	5	8	7	3	12	10	22
90+	1	1	1	3	2	4	6
40–90+	71	68	133	124	204	192	396
0–90+	151	166	133	124	284	300	584

lation the groups above twenty years of age. The time at disposal did not allow for the inclusion in the study of the group from 20 to 39 years of age in the villages. It was considered however that the numbers of this age group in Umanaq town were high enough for the purpose.

The delimitation of what may be described as "normal" in such a population is always difficult. In this case it was decided to neglect the frequently variegated descriptions of diseases and symptoms with which a suggestible and eye minded population would often reply to questions about previous severe eye diseases. Of eyes with thin corneal maculae forty were included. Since their tension was found to be distributed evenly about a mean value of 15.2 mm, i.e. almost equal to and at any rate not above the total average of 15.7 mm they were not excluded.

Schiotz tonometers are delicate instruments of limited precision. Schwartz & Ambler (1964) have convincingly demonstrated the errors in adjustment which could be found in five new certified tonometers. In 700 duplicate measurements applying all possible combinations it was found that the difference between the results obtained by means of the two tonometers which differed most from each other was on an average as much as 0.50 scale units. This corresponds to 1.4 mm Hg in the medium range and 2.0 in the important upper range. Consequently too much weight should not be attached to minor differences in the mean values obtained from different samples and the same applies to the values $\bar{x} + 2s$ and $\bar{x} + 3s$. But it does not invalidate the demonstration that differences exist between comparable sub groups in a sample as the present.

The weight used throughout the present study was 7.5 g. It was chosen especially because a weight of 5.0 g would necessitate a more frequent change to a heavier weight - at scale unit 4 and lower values (Becker & Schaffer 1965). Such a change over may introduce a spurious bimodality as shown by Hollow & Graham. Packer *et al* (1964) also used a 7.5 g weight. These authors draw attention to the tendency which is often met with in Schiotz tonometry towards a preference for whole rather than half scale unit readings which manifests itself in an uneven distribution curve with several maxima and minima. Such a tendency is clearly apparent in the large Finnish survey (Katavisto *et al*). In the present work it will be seen that the tendency has been eliminated to a reasonable extent since the most pronounced minima in the curves of fig. 4 correspond to scale units $8\frac{1}{2}$, 8 and 8 and the course of the curve in fig. 5 is quite smooth.

It would hardly have been possible to obtain the present results from Umanaq by means of an applanation tonometer of the Goldmann type. The working conditions are primitive. In a few cases persons had to be sought out in their homes and the measurements made on the sleeping platform.

The tension indicator was used from a desire to be able also by measuring on the applanation principle to delimit a group of persons with increased pres

a) Classification of the *physiognomy* of the person examined as being *Eskimoic* or "mixed" when judged at a distance before the colour of the eyes could be seen

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tures The results obtained will be dealt with in a subsequent article, but a simple evaluation from the point of view of measuring technique will be given

As regards the 79 eyes in which the applanation pressure was found by the tension indicator to be 21 mm Hg it is interesting to see the Schiøtz values Fig 6 shows such a comparison The mean value is near 21 mm but the dispersion is considerable

One of the reasons for this may be found in the low accuracy of the reading because of the low magnification ($\times 3$) and low light intensity of the instrument (Bruun Jensen 1968) It should be noticed however that Schwartz & Dell Osso (1966) found an only slightly smaller dispersion of the difference between paired applanation and Schiøtz measurements made on supine persons (2.54 mm Hg) They mention that the dispersion may in particular be caused by the fairly considerable dependence of Schiøtz tonometry on the rigidity of the eye Incidentally the authors found the applanation pressure in supine position to be on an average 3 mm higher than the Schiøtz value (and in sitting position 1.1 mm higher than the Schiøtz value confer Hollows & Graham in table 3) On this basis the dispersion found in the present small material can not be said to be surprising It is strange however that the mean value of the Schiøtz values found is actually approximately equal to the adjustment value 21 mm of the tension indicator

On the whole the author of the present study found the tension indicator to

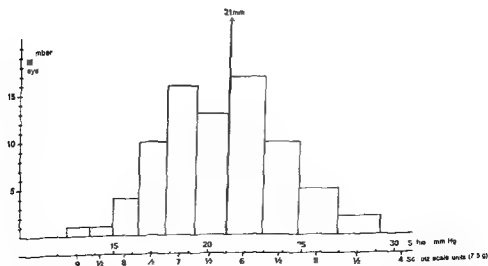


Fig 6

Tension indicator versus Schiøtz tonometer Distribution of Schiøtz intraocular pressure for 79 eyes with applanation pressure = 21 mm Hg (\bar{x} = 20.4 mm Hg $s.e.$ = 0.33 mm Hg s = 3.15 mm Hg)

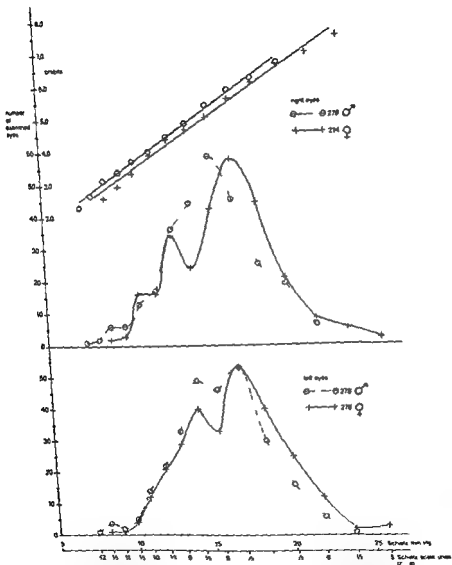


Fig 4

Intraocular pressure of normal eyes Separate curves for right and left eyes of men and women without diagnosis of glaucoma and without major corneal alterations i.e. tonometrically normal eyes. As regard right eyes distribution curves in probits show good approximation to straight lines.

be suitable for the purpose and more convenient to use than the Schiøtz tonometer. With improved optics and illumination it would be a very valuable instrument particularly under primitive conditions as in Greenland.

Conclusion

In a survey of the population of a medical district in Greenland with more than 95 per cent participation it has been shown that measured with a Schiøtz tonometer the mean tension of normal eyes in Greenlanders is 15.7 mm Hg with a standard deviation of 3.0 mm. The results correspond exactly to those found in surveys of other populations. An analysis of the sub groups of the sample concerned has further shown that the eyes of women above forty years of age show a significantly higher tension than those of men (mean values \bar{x} 16.35 mm and \bar{x} 15.1 mm) just as the dispersion in the case of this female group is slightly greater than that of the male group ($s^2 = 3.3$ mm Hg and $s^2 = 2.8$ mm Hg).

Summary

Motivated by our knowledge of the great part which glaucoma plays in the problem of blindness in Greenland – and directly occasioned by a number of severe glaucoma attacks – the author carried out a glaucoma screening in the district of Umanaq in 1967. More than 95 per cent of the population above twenty years of age in the town and above forty years of age in the villages took part.

The geography, population and health service of the district as well as the method and material of the survey are mentioned briefly.

On the basis of 1108 normal eyes the mean value of the normal tension is calculated in the two sexes and in different age groups. It is concluded that this population of mixed Eskimo-Caucasian origin as regards the parameters mentioned gives the same results as other population groups which have been studied. As elsewhere the ocular tension has been found to be significantly higher in women than in men in the age group above forty.

Finally the limitations incident to the Schiøtz tonometry used for the present study are discussed in relation to applanation tonometry and the results obtained by means of Bruun-Jensen's tension indicator according to this principle are mentioned.

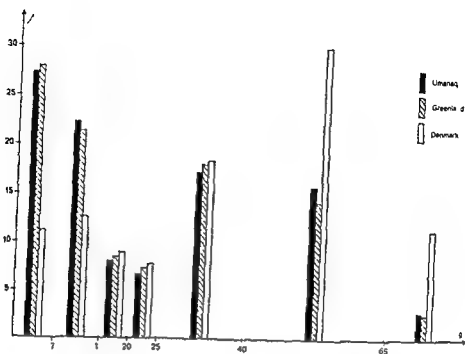


Fig 2

Percentage distribution of age from census 31 Dec 1965 (Number of inhabitants
Umanaq 2150 Greenland 35 117 Denmark 4 719 399)



Fig 3

Umanaq hospital with 33 beds in front of the mountain (11.5 metres) which dominates the island (Photo III Faurholt)

Acknowledgments

Department Nurse Eva Steenstrup Umanaq has given me invaluable assistance both as regards the actual examinations and in the arrangement of the material

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References

- Alsbræk P H & P Schiøler* Lægearbejde i Umanaq distrikt Ugeskr Læg 1969 101 619 625
- Alsbræk P H* Primary glaucoma in Greenland (Umanaq district) II Prevalence rates and case reports (in course of preparation)
- Armaly M F* On the distribution of applanation pressure I Arch Ophthal 1965 13 11 18
- Balyasnikova I V* Incidence of glaucoma in the Arkhangelsk region Vestn Oftal 1963 5 50 53
- Becker B* The decline in aqueous secretion and outflow facility with age. Amer J Ophthal 1958 46 731 136
- Becker B & R N Schaffer* Diagnosis and therapy of the glaucomas 2 ed Saint Louis The C V Mosby Company 1957 p 51
- Bertelsen A* Grønlandsk medicinsk Statistik og Nosografi Meddelelser om Grønland 1940 117-III a) 149 150 b) 155 156
- Bertelsen T M Davanger A Kolstad L Wirsching & H Aarved* Måling av det intraokulære trykk (Schiotz) og spaltelampeundersøgelse av personer i en større be drift T norske Lægeforen 1965 85 449 453
- Bjornsson G* The primary glaucoma in Iceland Acta ophthal suppl 91 1957
- Bruun Jensen J* An ocular tension indicator of the applanation type Acta ophthal 1967 45 546 551
- Bruun Jensen J* Glaucoma screening with Schiotz tonometer and tension indicator of applanation type Acta ophthal 1968 46 638 642
- Børresen P* Om Forekomsten af Glaucom og Blindhed i Grønland Ugeskr Læg 1956 88 194 195
- Clemmensen V* Personal communication 1969
- Clemmensen V* Problems in gonioscopic screenings in Greenland (in course of preparation)
- Davanger M* On the aetiology of glaucoma simplex Acta ophthal 1965 43 1 18
- Hert V* Meddelelser om Øjensygdomme i Grønland Ugeskr Læg 1929 91 805 806
- Hollows F C & P A Graham* The Ferndale glaucoma survey i L B Hunt Glaucoma symposium 1965 London Livingstone Ltd 1966 pp 24 44
- Kataavisto M* The diurnal variations of ocular tension in glaucoma Acta ophthal 1964 suppl 78
- Kataavisto M & I Sammalhti* Tonometry among persons over 40 years of age Acta ophthal 1964 42 310 377
- Leydhecker W A Akijama & H G Neumann* Der intraokuläre Druck gesunder menschlicher Augen Klin Mbl Augenheilk 1958 133 662 670

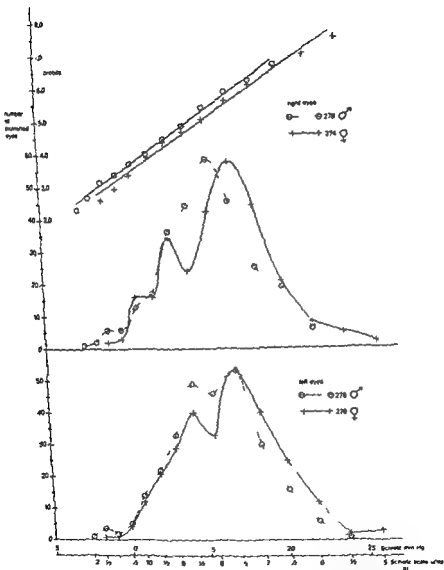


Fig 4

Intraocular pressure of normal eyes Separate curves for right and left eyes of men and women without diagnosis of glaucoma and without major corneal alterations i.e. tonometrically normal eyes As regard right eyes distribution curves in probits show good approximation to straight lines

- Linner E & U Stromberg Ocular hypertension (with discussion) : Glaucoma Tutzing Castle Symposium 1966 Basel/New York Karger 1967 pp 187 214
- Loh R. C. A. The problem of glaucoma in Singapore Singapore med J 1968 9 : 6-80
- Mann Ida Culture race climate and eye disease. Springfield Ill Charles C. Thomas 1966 pp 539 540
- Norman Hansen C M Ophthalmologiske Iagttagelser hos et arktisk Folk Hospitals tidende 1911 54 852
- Varikou K. Primary glaucoma as a cause of blindness Acta ophthal 1968 46 853 859
- Packer H A R Deutsch M W Devereux M Ashgarian & Ph M Lewis Frequency of glaucoma in three population groups J Amer med Ass 1964 155 123 127
- Pollack I P The challenge of glaucoma screening Surv Ophthal 1968 13 4 22
- Schwartz J Th & S S Ambler Comparability of a sample of certified Schiøtz tonometers Arch. Ophthal 1964 72 672 678
- Schwartz J Th & G G Dell'Osso Comparison of Goldmann and Schiøtz tonometry in a community Arch Ophthal 1966 75 783 795
- Skeller E Ojensygdomme i Grønland Ugeskr Læg 1949 111 529
- Skjoldsgaard H Grønlandske Blinde, i Landslægens Årberetning 1962 Beretninger vedr Grønland 1963 No 4 73 80
- Speakman J S personal communication to V Clemmesen 1968
- Steinsson A Glaucoma and heredity in Iceland Acta ophthal 1959 37 191 198

On account of small errors detected later on the actual deficit is slightly greater than the above mentioned six but the number of persons examined corresponds certainly to more than 95 per cent of the population of the district within the age groups concerned

5) Results

The necessary more detailed ophthalmological examinations and the evaluation of the results were made by V Clemmesen during a fortnight in August September 1967. As a final result the prevalence of angle closure glaucoma and open angle glaucoma was found to be 10 per cent (19/192) and 15 per cent (8/192) respectively among women and 0 per cent and 1 per cent (2/204) among men in the age group above forty. Out of the altogether 26 primary glaucoma cases 15 were not known before the screening. Principles of glaucoma classification and case records will be given in subsequent publications (Alsbrink Clemmesen).

Intraocular Pressure in Normal Eyes in Greenlanders Determined by Schiotz Tonometry

When all persons suffering from primary glaucoma (26) and all eyes (= 8) with severe alterations of the cornea and possible secondary glaucoma had been excluded the remaining number of eyes were 1108. The intraocular pressure was calculated on the basis of this sample. Fig. 4 and table II illustrate the results. The curves agree sufficiently closely with the Gaussian distribution to justify the use of the corresponding calculations. Since the intraocular pressures of the right and left eyes of a person cannot be considered as independent variables the calculations have been made separately for right and left eyes (conf. Hollands & Graham 1966). As it will be seen no difference was observed between right and left while there is a significant difference between the mean values for women and for men, the mean tension in female eyes being 16.1 ± 0.19 mm Hg as against 15.2 and 15.3 ± 0.17 mm Hg in male eyes. As will appear this difference between the sexes is evident in the age groups above forty but does not appear in the youngest group.

Measured by the standard deviation the biological dispersion in the group above forty is greater for women than for men and this difference is significant (most clearly with regard to left eyes $P < 0.01$).

Tension above $\bar{x} + 2s$ and $\bar{x} + 3s$ may be anticipated statistically in 2.28 and 0.14 per cent of normal eyes. These limiting values correspond in the case of men to 21.1 and 24.0 mm Hg and in the case of women to 22.4 and 25.6 mm Hg.

It was theoretically possible that the town population which was examined

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POLARIZING MICROSCOPIC STUDIES ON THE REGENERATION BEHAVIOUR OF PERFORATING CORNEAL WOUNDS

BY

MARGARET VARGA and J FEHÉR

The polarizing microscopic techniques came into prominence in the field of the morphological research in recent years. This fact can mainly be attributed to technical reasons.

The use of the so called "topooptical reactions" based on oriented colour binding considerably extended the possibilities of this technique and presented further informations to electron microscopic findings, one of the most important methods for submicroscopic structural research.

The development of the topooptical reactions was the result of Romhányi's work (1966). We can give its essentials as follows:

Treating the preparations with suitable colouring agents of molecular configurations (toluidin blue, rivanol, azur, methylen blue, thiosin etc.) the molecules of the colouring agents will link to each of the constituents of the preparation in a patterned array. The oriented binding of the colours results in a change of the anisotropy of the structure. The initial birefringence will increase or decrease possibly reverse. The topooptical reactions indicate very poor or even latent birefringences selectively. Topooptical reactions by polarizing optical techniques make possible the study of a number of structural peculiarities which hitherto were unaccessible. Thus the structure of the interfibrillar substance of the connective tissue and the peculiarities of the lipoprotein membranes etc. could be better understood.

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Table II
Intraocular pressure of normal eyes by Schiøtz tonometer

Age group		Women		Men		Comparison between women and men Significance test
		right	left	right	left	
0-39	\bar{x}	15.8	15.5	15.7	15.5	$P_1 < 0.2$
	$s.e.$	2.9	2.8	3.0	3.3	
	n	107	107	80	80	
40-49	\bar{x}	16.2	16.3	14.7	14.8	$P = P_1 < 0.005$ $P_1 < 0.05 < P_r < 0.1$ $P < 0.05 < P_1 < 0.1$
50-59	\bar{x}	16.4	16.3	15.4	15.6	
60+	\bar{x}	16.2	16.2	15.0	15.2	
40+	\bar{x}	16.3	16.4	15.0	15.2	$P_r = P_1 < 0.0005$ $P_1 < 0.01 < P_r < 0.05$
	$s.e.$	0.25	0.26	0.20	0.19	
	s	3.3	3.4	2.8	2.7	
	n	167	169	193	200	
20+	\bar{x}	16.1	16.1	15.2	15.3	$P < 0.001 < P_1 < 0.005$ $P_r = P_1 < 0.2$
	$s.e.$	0.19	0.19	0.17	0.17	
	s	3.1	3.2	2.9	2.9	
	n	214	216	218	250	

\bar{x} = mean value (mm Hg)

$s.e.$ = standard error of mean (mm Hg)

s = standard deviation (mm Hg)

n = number of eyes examined

P = probability (for right eyes two tailed test)

P_1 = probability (for left eyes two tailed test)

(P values according to Student distribution for degrees of freedom ≤ 200)

P values according to normal distribution for degrees of freedom > 200

Tables Documenta Geigy B ed Basel 1962)

during the dark period might have displayed intraocular pressures which differed from those of the inhabitants of the villages who were as mentioned examined in the summer. It might be imagined for instance that an effect similar to that of a dark room test on many narrow angles would result in a higher intraocular pressure in the group observed during the dark period or that other seasonal factors might influence the tension. However the present results do not support any theories of that kind the mean tensions differing

These examples suggest the method renders it possible to study areas which are difficult to access by other techniques

The polarizing optical methods were used in studying the collagen fibres of the stroma and keratocytes.

1 The study of the collagen fibres

a) Protein fibrils

The phenol reaction is very useful to study the protein fibrils of the collagen. This is one of the earliest polarizing optical techniques (Ebner 1894). The phenol molecules being built in between the adjacent keto imido groups of the protein chains of the collagen fibrils reverse the initially positive birefringence to negative simultaneously increasing it. The phenol reaction is specific to the collagen.

b) Interfibrillar substance

Consists of biochemically acid mucopolysaccharides called often by different authors as ground substance "Kittsubstanz" and is believed to be amorphous. Romhányi (1963) verified the structural characteristics of the interfibrillar substance with polarizing optical techniques. His results indicate that acid mucopolysaccharide chains are parallelly arranged to the fibrils of the intra and interfibrillar substance. Various basic colour agents mostly toluidin blue and rivanol enlighten the study of the interfibrillar substance (by polarizing optical techniques) by binding isolatedly to it.

Information is furnished on the fibril forming process by the phenol reaction and on the forming of the interfibrillar substance by the toluidin blue and rivanol staining (anisotropic staining) respectively.

2. The study of the keratocytes

a) Examination of the structural lipoids

Romhányi & Deak (1961) developed the topo-optical reactions which give the opportunity of studying the lipo-protein membranes by polarizing optical techniques. They used various basic colour agents with an after treatment by potassium ferricyanide or by a mixture of potassium iodide-potassium ferricyanide. The after treatment fixes the colour linkages on the structure. In the topo-optical reactions of the lipoprotein membranes the protein part of the membrane and the lipoids as well are responsible for the binding and the orientation of the colouring agent respectively. The method is useful for studying basal membranes, cell membranes, ergastoplasm, mitochondria and other cytomembranes.

b) Examination of the activity of the keratocytes

The anisotropy of the keratocytes became evident during the studies of the cornea for other purposes. This casual observation gave us the impulse to study

hours After 3-4 days the patients were sent home The first pigmentations are then in most cases already clearly visible in the borders of the coagulated areas After a fortnight the patients were allowed to return to work

In two cases the method has been used to complete the delimitations of detachments operated upon after Custodis with cryo treatment under the silicon plomb In one case with aphacia a small flat detachment with two peripheric tears was circumscribed All cases of retinal ruptures with and without detachment have healed completely without complications and with unchanged or improved vision

Recently we have begun to treat diabetic retinopathy both cases with proliferative vessels on the disc and cases with other alterations of the fundus In these cases retrobulbar anaesthesia with Xylocain® 2% with epinephrine has been given The results seem promising but the observation time has been short

In all cases treated with the Fankhauser Lotmar device no complication whatsoever has occurred The apparatus has worked with great safety and reliability and has never failed The method has proved much easier than the usual photocoagulation with the Zeiss apparatus in the hand of a trained biomicroscopist All cases of retinal detachments and ruptures have healed and no recurrences have occurred The apparatus will soon be made for sale** It has proved to be an excellent device for rapid and exact photocoagulation first and foremost in cases with extremely peripheric lesions in which Eisner's funnel can be of good help but also in lesions of the central fundus

Summary

Photocoagulation with the device of Fankhauser and Lotmar is described The great advantages of this method over the usual photocoagulation especially in cases with peripheric lesions are emphasized

References

- Fankhauser C Attachment for Goldmann Three Mirror Contact Glass For examination of the retina serrata and periplazm *Amer J Ophthal* 61: 467 1961
Fankhauser C & Lotmar H Photocoagulation through the Goldmann Contact Glass
AMA Arch Ophthal 63: 196

Lithicron (Astra-Sweden)

Manufactured by SADIAMEL, Rue Jardinere 130 La Chaux-de-Fonds Switzerland

Eisner's funnel slightly modified. The indentors of different lengths are interchangeable

Fig 3



tact glass is made very easily. By using Eisner's indentor funnel (Fig 3) which is to be slipped over the contact glass photocoagulation is possible without any difficulty even on the pars plana in cases with clear lenses. This funnel offers two advantages (1) the eyeball is immobilized by suction and (2) the sclera may be indentated at variable distances from the ciliary body. A red spot in the slit image on the retina indicates the area to be coagulated. An inbuilt cobalt blue filter makes coagulation possible during fluorescein angiography. Even in cases with cataract clear zones between the cataractous spokes may be used for photocoagulation by slightly tilting the contact glass.

In 11 eyes 14 peripheral retinal ruptures without detachment but with marked vitreous tractions have been treated. All these ruptures were complications to an acute posterior vitreous detachment. In one eye multiple breaks after a fusion were coagulated. In many cases the tears were so peripheral that coagulations had to be made on the pars plana with the aid of Eisner's funnel to circumscribe the lesions. The ruptures were easily found in all cases and treated without difficulty. In most cases the field stop on the Zeiss photocoagulator was put on 1.5° corresponding to 3.6° (1.06 mm) when the Fankhauser-Lotmar device is used or more seldom on 0.5° corresponding to 1.2° (0.35 mm). The intensity "red II" of the photocoagulator was used in most cases. Only in a few dark fundi was red I chosen. The iris stop of the coagulator was used fully open. The high intensity makes the use of very short times possible which is of importance since the eye treated is immobilized only by the contact glass. In all cases with peripheral retinal ruptures local anaesthesia with Novesin® 0.4% was used. After the treatment the patients were kept in bed for about 24

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- Kitano S & Goldman J N* Cytologic and histochemical changes in corneal wound repair *Arch Ophthalmol* 76 345-354 1966
- Nemeth I* Das reticuloendotheliale System des Auges mit Rücksicht auf die eiterigen Hornhautentzündungen *Klin Mbl Augenheilk* 96 613-631 1936
- Payrau P, Poliquen Y, Faure J P & Offret G* La transparence de la cornée *Masson et Cie Éditeurs Paris* 1967
- Pullinger B D & Mann I* Avascular healing in the cornea *J Path Bact* 55 151-158 1943
- Robb R M, Kuwabara T* Corneal wound healing II An autoradiographic study of the cellular components *Arch Ophthalmol* 72 401-408 1964
- Romhányi Gy* A polarisációs mikroszkópia szerepe a submikroszkopos szerkezetek kutatásában *Morph Ig Orv Szemle* 2 1-30 1962
- Romhányi Gy* Über die submikroskopische strukturelle Grundlage der metachromatischen Reaktion *Acta histochem* 15 201-233 1963
- Romhányi Gy* A koloszovet sejtkezelti állományok ultrastrukturájáról topooptikai reakciók polarisációs optikai vizsgálata alapján *Thesis Pecs* 1966
- Romhányi Gy, Deák Gy* Ultrastructure of the ergastoplasm of pancreas acinar cells as revealed by topooptical staining reactions *Acta Bioch et Biophys Acad Sci Hung* 2 (2) 115-129 1967
- Salzer F* Wie regeneriert sich eine Hornhautlücke? *Klin Mbl Augenheilk* 107 389-404 1941
- Weimar V L* The transformation of corneal stromal cells to fibroblasts in corneal wound healing *Amer J Ophthalmol* 44 173-182 1957
- Weimar V L* The sources of fibroblasts in corneal wound repair *Arch Ophthalmol* 60 93-109 1958
- Weimar V L* The role of epithelium in corneal wound repair *Trans N Y Acad Sci* 21 582-584 1959
- Weimar V L* Healing process in the cornea. In *Duke Elder S & Perkins E S* The Transparency of the Cornea Symposium Blackwell Oxford Masson et Cie Paris 1960 111-124
- Weimar V L* Effect of amino acid, purine and pyrimidine analogues on activation of corneal stromal cells to take up neutral red *Invest Ophthalmol* 1 226-232 1967
- Weimar V L, Haraguchi H K* The development of enzyme activities in lag corneal connective tissue cells during the phase of wound repair I 5 nucleotidase and succinic dehydrogenase *Invest Ophthalmol* 4 853-866 1965
- Weimar V L, Davis M & Haraguchi K H* Instantaneous and 30-90 minute reactions of cells to injury *Exp Cell Res* 39 10-21 1965
- Weimar V L & Haraguchi K H* The development of enzyme activities in corneal connective tissue cells during the lag phase of wound repair II Formalin resistant oxidase like reaction *Invest Ophthalmol* 5 14-21 1966

keratocytes between the swelled fibres compared with the intact areas seemed unchanged or slightly decreased

After 12 hours In relation to the previous state no deviation was evident by polarizing optical technique

After 24 hours (Fig 1) The corneal stroma swelled the anisotropy of the fibres unchanged The anisotropy of the keratocytes adjacent to the edges of the wound increased The shape and size of the keratocytes practically agreed with those of the intact area except for the increased birefringence

After 48 hours (Fig 2) The swelling of the stroma has not changed The area between the edges of the wound reveals isotropy with very poor birefringence of the clumped fibrin here and there

The increased anisotropy of the keratocytes could be observed in the stroma close to the wound The keratocytes were slightly widened and lengthened These phenomena could be found in the neighbourhood of the wound only keratocytes did not display any changes at all beyond that toward the limbus

After 7 days (Fig 3) The neighbourhood of the wound was swelled the fibres were loosened The upper quarter of the area between the edges of the wound was filled with penetrating epithelium processes Under this area the



Fig. 1

The increased anisotropy of the keratocytes becomes evident among dark compensated fibres C R 1 comp Polar micrograph Toluidin blue colouring Abt 800 X

Eye Clinic Medical Faculty Rotterdam

VARIABILITY OF THE ELECTRO OCULOGRAM (EOG)

BY

G H M VAN LITH and J BALIK

Introduction

Electro oculography developed by Arden in 1962 is a useful and worthwhile method in clinical practice

By measuring not the standing potential itself but the increase during light adaptation as expressed in the light peak dark trough ratio (LP/DT ratio) individual variations are diminished Nevertheless variations between individuals and in the same individual are rather high (Elenius 1962 Kelsey 1967) As the variations in the EOG when determined in one and the same person are important in view of the check on chloroquine intoxication a confirmation of Kelsey's data seems valuable A preliminary report was already published (Henkes *et al* 1968)

Method

Examination was done in 15 normal subjects (9 ♂ and 6 ♀) varying in age from 21 to 48 From each of them 10 EOG's were obtained according to Arden's technique on different days and different daytimes in the course of some weeks The light peak dark trough ratio which normally is about 2.00 with a lower limit of the normal range of 1.85 was calculated (Arden 1962)

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the problem (Feher & Varga 1969) It was found that the lipoprotein lamellas of the cell organella (ergastoplasm mitochondrium etc) are responsible for the anisotropy of the keratocytes The possibility to examine the organella by polarizing optical means is due to the fact that the organella are arranged length wise even in the longitudinally extending cells as well shown by electron photomicrography The quantity of the cell organella may be concluded from the extent and degree of the anisotropy In turn the quantity of the organella is indicative for the metabolism or activity of the cell

On the basis of the above considerations the activity and fibroblastic function of the cell might be deduced from the anisotropy of the keratocytes

Material and Methods

Perforating lesions were made on the central area of the corneas of 28 rabbits, 3 mm of length in each case

The eyes were enucleated after 2 12 24 48 hours and 1 2 4 weeks respectively The removal of the eyes was then followed by processing with polarizing optical techniques

The globes were fixed in neutral formol of 1:4 Refrigerated sections were cut of 10 μ thickness partly after having been embedded in gelatine and partly without gelatine

The native examinations were executed after covering with acaci gum and glycerol

Topo-optical reactions phenol reaction according to Ebner (1894) rivanol colouring according to Romhányi 1962 (Rivanol 0.1 Mol precipitated with potassium ferricyanide of 2%) colouring with toluidin blue according to Romhányi 1962 (toluidin blue colour solved in Michaelis veronal potassium acetate buffer of 3.5–6 pH to 0.01 % concentration precipitated with potassium ferricyanide of 2% or with a mixture of 1:7 from potassium ferricyanide and potassium iodide)

The extraction of the lipid was accomplished in a mixture of 3:1 chloroform:metanol during 24 hours in room temperature

Observations

After 2 hours The corneal stroma adjacent to the wound swelled approximately to the double Changes of anisotropy were not perceptible The anisotropy of the

Results

The variability per individual was rather high Figure 1 gives an impression of this variability For each subject the mean value and the standard deviation were determined for the right and left eye separately (figure 2) The mean value of subject 15 proved to be significantly higher than those of the other subjects This difference is statistically verified For this reason the results of this subject were omitted in further calculations The mean value and standard deviation of all 140 experiments were respectively 2.15 and 0.25 These results are of the same order as Kelsey's

With these experiments as a basis two conclusions can be drawn When only one EOG is determined values below 1.85 cannot be said to be abnormal To be sure if the result is pathological two times the standard deviation has to be subtracted from the mean value and to be quite sure even three times the standard deviation This means that a value lower than 1.65 is highly probably abnormal an α value lower than 1.40 surely is Values between 1.65 and 1.90 are borderline cases The second conclusion is that an alteration of the EOG lower than 0.25 in the same person has no particular meaning An alteration of more than 0.25 is remarkable of more than 0.50 is of much value

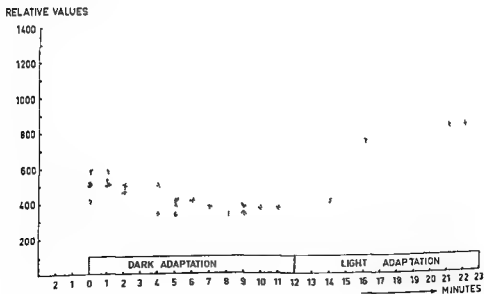


Fig 1

Standing potentials measured and plotted in relative values during 12 minutes dark adaptation and 12 minutes light adaptation Before dark adaptation the subjects are light adapted during 10 minutes

fibroblast mass was surrounded by a substance of mucoid character. Some very fine fibrils were seen crossing the mucoid substance. Near the edges of the wound there was a number of active keratocytes among the parted stroma fibres.

After 14 days The area between the edges of the wound was filled with cicatrized tissue crossed only by thin collagen bridges (fig 4) which were arranged corresponding to the original fibre pattern. Between the collagen fibrils however abundant mucoid substance was shown following the regular fibre arrangement (fig 5). Numerous fibroblasts were seen in the freshly grown connective tissue (fig 6). The fibres of the stroma adjacent to the wound were still swollen among them a number of elongated thickened keratocytes of strong anisotropy.

After 28 days The collagen fibrils were increased and strengthened in the cicatrized tissue between the edges of the wound (fig 7). The interfibrillar substance too was oriented along the fibres. As before there were many fibroblasts in the cicatrized tissue. The stroma swelled in the vicinity of the wound. Among the fibres there were many keratocytes in the area corresponding to the swollen stroma with widened and elongated plasma showing strong anisotropy (fig 8).

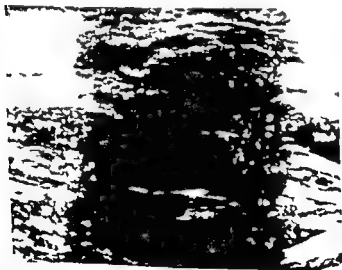


Fig 4

Thin collagen fibrils between the edges of the wound. Polar micrograph.
Phenol reaction. Abt 600 X

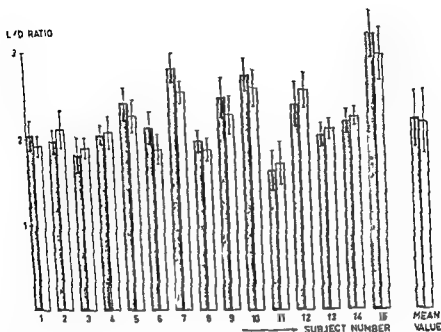


Fig. 2

Mean values and standard deviation (vertical bar) of the light peak/dark trough ratio of 10 experiments in each of 15 subjects (shaded block right eye white block left eye)

Causes of variability

In order to diminish these great variations their possible causes were examined

The position of the electrode surely alters the height of the standing potential. If only the I P/DT ratio is measured no essential influence can be expected. To check this point 5 EOG's were determined in 9 subjects directly after each other with the electrodes remaining at the same place in one afternoon. Only the results of those 5 subjects from whom also 10 EOG's were determined on different days are given in the table. The standard deviations of the 5 EOG's made in one afternoon appeared to be not smaller than those of the 10 EOG's. The conclusion must be that replacing the electrodes is not very influential.

A peculiar phenomenon was that the 2nd and 5th EOG were always higher than the others. The difference between the 1st, 3rd and 4th EOG was not statistically significant. A clear explanation for the high values obtained in the 2nd and 5th EOG cannot be given.

A second variable factor may be the adaptive state before the darkadaptation time starts. From literature (Kris 1960) it is known that — like the increase



Fig 2

Elongated keratocytes among the corneal fibres The fibres are dark the keratocytes are compensated to brightness G R I comp Polar micrograph Toluidin blue colouring Abt 800 X

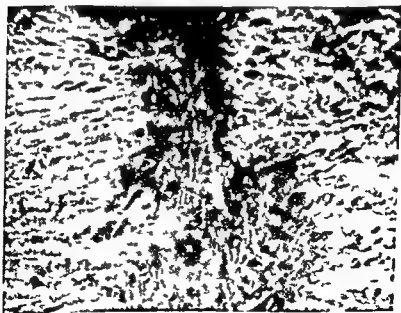


Fig 3

Fibroblast mass between the edges of the wound Much active keratocytes are between the aparted fibres Polar micrograph Toluidin blue colouring Abt 400 X

Table 1

subject number	mean of 10 X	stand dev	mean of 5 X	stand dev
10	2.62	0.20	2.67	0.19
11	1.64	0.23	1.84	0.14
12	2.42	0.24	2.95	0.16
13	2.04	0.13	2.37	0.12
14	2.17	0.13	2.64	0.26

during lightadaptation – also an increase can be observed going from the light adapted state to the darkadapted state. Such an increase may interfere with the light peak dark trough ratio which has to be measured. Therefore in 5 subjects the standing potential has been measured in 13 experiments while in stead of light adaptation after 12 minutes the lights stay off. Before dark adaptation the subjects were light adapted during 10 minutes.

Figure 3 is an example from one subject. For the 5 subjects the mean increase was between 0.348 and 0.387 and was significant at a 1 per cent level. Because this increase occurs at the same time as normally the light peak can be

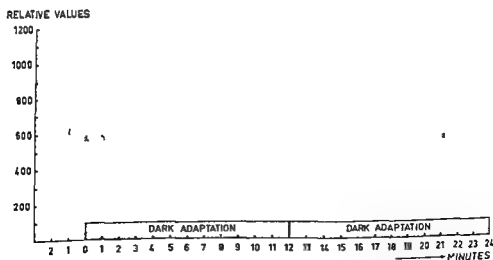


Fig 3

Standing potentials in relative values during 24 minutes dark adaptation. Before dark adaptation the subjects are light adapted during 10 minutes.

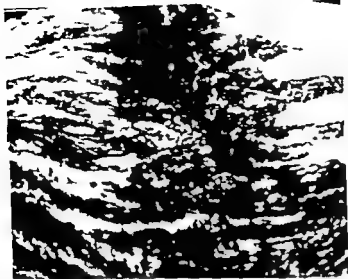


Fig 7

Thickened and multiplied collagen fibrils between the edges of the wound Polar micrograph Phenol reaction Abt 600 X



Fig 8

Enormous number of fibroblasts in the scar tissue and the surroundings Polar micrograph Toluidin blue colouring Abt 600 X

expected it will be clear that the adaptive state before dark adaptation starts is an important factor

To see whether the time of day was of influence all experiments were grouped according to day hours (fig 4) Correlation was determined by mean of Spearman's coefficient of correlation ($R = 0.708$) This means that variability during the day is proved for 50 per cent Hence if possible one should try and examine and re examine the patients during the same time of the day

Other factors which may be involved with the great variations occurring in EOG examinations are difficult to measure or to prevent For instance the change in the electrical resistance of the skin dependent on the degree of perspiration the possible occurrence of a flood of tears making contact with the nasal electrode and the ability to keep the eyes open during the early minutes of light adaptation The last mentioned factor may influence the rapidity of retinal bleaching and so the height of the light peak in the EOG

A last factor causing variations in the EOG finally is the patient's self control in moving only his eyes and not his head

Summary

Variability of the EOG has been determined by making 10 EOG's in each of 15 normal subjects The mean value and standard deviation of the experiments was respectively 2.15 and 0.25 From the results two conclusions have been

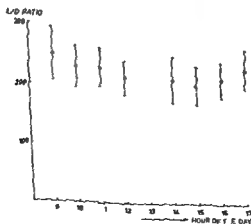


Fig 4

Light peak dark trough ratio according to day hours Vertical bars Standard deviation.



Fig 5

The interfibrillar substance in the cicatrized tissue shows distinct anisotropy Polar micrograph Toluidin blue colouring Abt 600 X

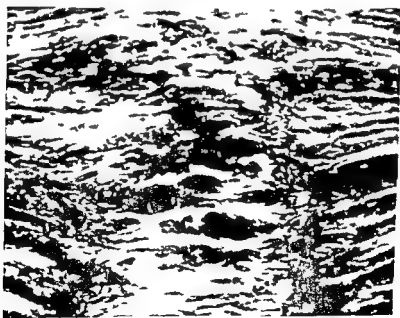


Fig 6

The fibroblasts in the scar tissue and the surroundings exhibit strong anisotropy G R I comp Polar micrograph Toluidin blue colouring Abt 600 X

drawn Firstly values lower than 1.65 are highly probably abnormal lower than 1.40 surely are Secondly only an alteration of the EOG of more than 0.25 in the same person has particular meaning

Some factors which may cause these rather great variations have been examined

References

- Arden G B & Barrada A Analysis of the electrode oculograms of a series of normal subjects *Brit J Ophthal* 46 468-482 1962
- Arden G B Barrada A & Kelsey J H New clinical test of retinal function based upon the standing potential of the eye *Brit J Ophthal* 46 449-467 1962
- Arden G B & Kelsey J H Some observations on the relationship between the standing potential of the human eye and the bleaching and regeneration of visual purple *J Physiol* 161 205-226 1962
- Arden G B & Kelsey J H Changes produced by light in the standing potential of the human eye *J Physiol* 161 189-204 1962
- Elenius V & Lehtonen J Spectral sensitivity of the standing potential of the human eye *Acta Ophthalm* 40 559-566 1962
- Henkes H E van Luth G H M Gaisner P D & de Haas J P Electrodiagnostic procedures in diabetes In Clinical value of electroretinography ISCERG Symp Ghent 1966 393-402 Karger Basel/New York 1968
- Kelsey J H Variations in the normal electro oculogram *Brit J Ophthal* 51 44-49 1967
- Liss C Vision Electro oculography In Medical Physics vol 3 692-700 Year Book Publishers Chicago 1960

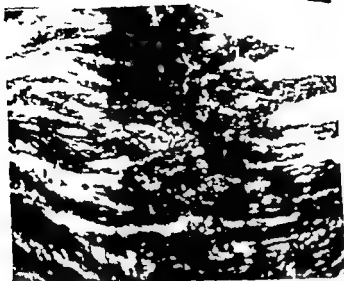


Fig 4

Thickened and multiplied collagen fibrils between the edges of the wound Polar micrograph Phenol reaction Abt 600 X



Fig 8

Enormous number of fibroblasts in the scar tissue and the surroundings Polar mic ograph Tolu din blue colouring Abt 600 X

Eye Clinic Medical Faculty Rotterdam

THE INFLUENCE OF GLUCOSE LOADING ON THE ELECTRO OCULOGRAPHIC RATIO (EOG) IN NORMAL SUBJECTS AND DIABETICS

BY

J BALIK and G H M VAN LITH

Introduction

The determination of the light peak dark trough ratio (LP/DT ratio) in the EOG can be a suitable supplement of a general functional examination in diabetes mellitus. The standing potential is usually low, mostly it shows a greater decrease in long term diabetes with serious diabetic retinopathy.

The LP/DT ratio 100 is found to be lowered, the light peak time often delayed (6). A correlation between the LP/DT ratio and the blood sugar level after an oral glucose tolerance test could not be proved (4). However, after an intravenous glucose infusion reaching much higher blood sugar levels it appeared that in normal individuals the LP/DT ratio increased significantly while in diabetics it did not (5).

Only a small number of eyes was examined at that time. Limiting the investigation only to the EOG we have now examined and compared a larger group of diabetics and normal subjects.

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Discussion

Following perforating corneal injuries the healing of the stroma takes its course with cicatrization. The fibroblasts are responsible for the forming of the cicatrized tissue. The origin of the fibroblasts has been the subject of much discussion.

According to the observation of *Weimar* (1957, 1958, 1959, 1960, 1962, 1963, 1966) 24 hours after the lesion about 75 per cent of the keratocytes transform into fibroblasts in the surroundings of the wound. By histochemical examinations *Kitano* (1966), *Kitano & Goldman* (1966) proved that all the fibroblasts which contributed to the healing of the wound originated from the transformation of the keratocytes.

In addition, it was assumed that the transformation of other cells (first of all macrophages) is responsible for the formation of fibroblasts (*Pullinger & Mann* 1943, *Duke-Elder* 1954, *Weimar* 1958). The macrophages originated partly from the monocytes of the blood, partly they were histiocytes of RES origin (*Nemethi* 1936, *Boros & Takats* 1951). *Salzer* (1937) assumed that the fibroblasts may develop from the transforming epithelial cells.

Autoradiographic investigations of *Robb & Kuwabara* (1964) have shown that the epithelial cells of the cornea never transformed into fibroblasts and when the corneal wound is situated in the central area the mononuclear cells do not contribute to the healing. In the case of peripheral wounds the authors do not preclude this possibility.

The first sign of the beginning of the production of cicatrized tissue is the increasing activity of the keratocytes. The activating factor(s) are produced by the injured epithelium (*Weimar, Davis & Haraguchi* 1965). In the activated keratocytes there begins a strong metabolic function with newly developed enzymesystems.

During our studies changes could be observed by polarizing optical techniques as soon as 24 hours after the lesion. The anisotropy of the keratocytes near to the wound increased without a change of the shape or size of the cell. The anisotropy of the keratocytes is due to the cell organella, hence the increasing anisotropy indicates the growing of the former and the more intense metabolic activity as well. The keratocytes after 48 hours become longer and broader with forms exhibiting mitotic activity.

Dunnington & Smelser (1958) proved that the synthesis of the mucopolysaccharides begins with the activation of the keratocytes. By using autoradiography they observed the take up of S^{35} labelled sulphate in the narrow zone surrounding the wound 24 or rather 48 hours after the lesion, which fact was an evidence for the synthesis of sulphated mucopolysaccharides. The fibre synthesis equally begins with the production of the ground substance.

On the second day the fibroblasts are beginning to synthesize the collagen

Methods

FOG was examined by means of Arden's technique (12) in 16 normal persons (27 eyes - 15 men aged 22 to 50 and 1 woman of 28) and in 20 diabetics (39 eyes - 9 men and 11 women varying in age from 33 to 63).

Firstly the EOG was determined without glucose loading. After this initial examination 500 ml 30 per cent glucose solution was given in 45 minutes during which time the second FOG was determined. The blood sugar level was examined before the first LOG, after the DA time of the second EOG (approximately halftime of the glucose infusion) and at the end of the second FOG (approximately at the end of the glucose infusion) by means of the glucose oxidase method. The mean value of the latter two findings was taken into consideration. As the value after glucose loading also depends on the value before glucose loading only the difference in both values was taken into account and verified by means of Student's *t* test.

Qualitative changes (increase or decrease of the EOG) in both groups were verified by means of the χ^2 test. The correlation between the EOG and the difference of the blood sugar levels in the loading tests was determined by Spearman's correlation test. The results of the examination of both groups are given in the table; the statistical results in the text.

Results

The difference of the mean value of the LP/DT ratio between the control and the diabetic group before loading was 49.7. This difference is statistically significant ($t = 4.920 > 2.043$ for 66 degrees of freedom). Also the variance

Table 1

LP/DT ratio	decreased	increased	
diabetics	4	23	27
control	23	16	39
	27	39	66

precursor. At first this soluble substance of proteom character is secreted into the extracellular spaces and then aggregates into a fibrous structure.

According to our examinations on the sixth day following the lesion the area between the edges of the wound is filled up with a cell mass consisting of fibroblasts. Among the fibres of the swollen collagen adjacent to the wound there are a number of fibroblastic transformed keratocytes. The fibroblasts are surrounded by mucoid substance in which sparse fibrils can be detected by polarizing technique.

In the later stages of the regeneration the growing of the fibroblasts and the increase of the cicatrized tissue become evident. At first in the newly formed cicatrized tissue there are few fibrils but then they increase in number more and more. The fibrils are thickened gradually and follow the pattern of the intact fibres. The arrangement of the fibres in the scar is possibly due to the force exerted by the intraocular pressure to the cornea (Payrau *et al* 1967). The ranging of the fibres is accompanied by the gradual clearing off of the scar.

Summary

The authors investigated the perforating corneal wound in the central area by polarizing optical techniques. The results show that the phenomena of regeneration originate from the keratocytes of the stroma near the wound. The activity of the keratocytes increases: the cells multiply and their fibroblastic activity produces the scar tissue. The collagen fibres gradually grow and strengthen in the mucoid of the cicatrized tissue.

References

- Boros B & Takats I: Untersuchung der Widerstandsfähigkeit des Hornhauttransplantats Infektionen gegenüber bei besonderer Berücksichtigung der Rolle des Reticulo endothels. *Acta ophthal (hbb)* 2/ 499-503 1951
- Duke Elder W S: Text Book of Ophthalmology Vol 6 London Henry Kimpton 1954 601-6013
- Dunnington J H Smelser G A: Incorporation of S^m in healing wounds in normal and devitalized corneas. *Arch Ophthal* 60 116-129 1958
- Ebne W: Über eine optische Reaktion der Bindesubstanzen auf Phenole. *Sitzungsber Akad Wiss Wien Kl Abt 3* 169-188 1894
- Feller J Varga M: A keratocyták submikroszkopos structurája polarizációs optikai és elektronmikroszkópos vizsgálatok alapján. In press
- Altano S: Cytoplasmic granules of the corneal stromal cell. *Invest Ophthal* 5 277-287 1966

difference of both groups ($F = 2.6$ for 28 and 38 degrees of freedom) shows a difference between the normal subjects and the diabetics

Examining the control group in the fasting state (27 eyes) the mean value of the LP/DT ratio was 211.9 (standard deviation 47.6) after glucose loading the ratio was increased by 23.6 (standard deviation 41.6) this increase is statistically significant ($t = 3.06$ for 28 degrees of freedom) The correlation factor R between the increase in the LP/DT ratio and the blood sugar level was 0.50 ($\Delta 1.96 = 0.46452 < 0.50$)

The mean value of the LP/DT ratio in the diabetic group before glucose loading (39 eyes) was 162.3 (standard deviation 29.1) after glucose loading the mean increase was 2.7 (standard deviation 30.9) This increase does not differ from zero ($t = 0.545$ for 38 degrees of freedom) The correlation factor R between the amount in which the LP/DT ratio and the blood sugar level increase after loading was 0.115 ($0.539 -$ statistically not significant) $\chi^2 = 1.0810$ for 1 degree of freedom By means of this test it is statistically proved that the LP/DT ratio increases during glucose loading more often in the control group than in diabetics

Discussion

From these results we can conclude that the LP/DT ratio in the EOG is lower in diabetics than in a control group. While in the control groups this ratio is increased significantly and quite often by means of intravenous glucose infusion it does not increase in diabetics it even decreases sometimes. The increase in the LP/DT ratio of the control group has not a significant correlation with the increase in the blood sugar level during the loading.

It is rather difficult to explain exactly the changes found because little knowledge exists about the nature of processes which determine the height of the standing potential and its alteration during light adaptation. If we consider that the EOG originates in the border layer between retina and chorio-capillaris (in the pigment epithelium) and that it can be changed by influences on both sides (7) we can possibly explain the results obtained by means of theoretical knowledge of the difference in metabolic processes which exist between the normal and diabetic retina. Both retinas are insensitive to blood sugar changes and to the presence of insulin (3). This explains why only a small, perhaps no correlation exists between the LP/DT ratio and the blood sugar level.

However changes in secondary metabolic glucose processes (energy shifting during phosphorylation and changes in the relation between oxidized and

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DENDRITIC (HERPETIC) KERATITIS

I. Incidence – Seasonal Variations – Recurrence Rate – Visual Impairment – Therapy

BY

M. S. NORN

Herpetic keratitis is a frequent disease often causing lost working days. The disease represents a steadily increasing problem within our highly advanced social system where other diseases are combated with greater success.

The present possibility of instituting rational treatment with 5-iodo-2-deoxyuridine (IDU) which interferes directly with the viral metabolism is regarded as a great improvement.

Numerous reports have been published on this subject since Kaufman *et al.* (1947) introduced IDU treatment against dendritic keratitis. A favourable result has been noticed in most cases (Kaufman, Inseth *et al.*, Capperucci, Mach *et al.*, Laibson *et al.*, Maxwell, Patterson *et al.*, Sood *et al.* etc.).

The response to IDU has been studied through double-blind trials using as placebo water or substances of at least doubtful therapeutic value.

These trials have shown IDU to give more rapid cure than placebo (Patterson, Laibson, Jepson, Hart *et al.*, Davidson, Burns).

Fy *et al.* and Mackenro took up a more reserved attitude. The latter found cauterisation to have a better effect than IDU. Calkes found no significant difference between the effects of iodine cauterisation and IDU therapy.

Some workers state that a favourable response to IDU is only obtainable

- Fankhauser F Lotmar W & Poulter A* Photocoagulation Through the Goldmann Contact Glass II An Apparatus Using a Quasi Continuous Laser Source AMA Arch Ophthal 79 674 1968
- Fankhauser F Lotmar W & Roulier A* Photocoagulation Through the Goldmann Contact Glass III Clinical Experience With an Apparatus Using a Quasi Continuous Laser Source AMA Arch Ophthal 79 684 1968
- Fankhauser F & Lotmar W* Methods of Photocoagulation Through the Goldmann Contact Glass Mod Probl Ophthal vol 7 pp 256 272 (Karger Basel/New York 1968)
- Linder B* Acute Posterior Vitreous Detachment and Its Retinal Complications Acta Ophthal (Kbh) Supplementum 87 (Munksgaard Copenhagen 1966)

reduced coenzyme nicotinamid adenin dinucleotid in oxidizing of fat acids) can influence the normal semipermeable membrane causing an increase in potential difference on either side of the membrane. This may explain the increase in the standing potential of the normal retina during light adaptation and in the LP/DT ratio after glucose loading.

In diabetes permeability of the capillary membrane is increased. This results in a free and uncontrolled transport of water and ions. Also the ability to maintain differences in concentration supported by means of released energy during the glucose metabolism and redox potential changes is diminished. Because in this situation the secondary metabolic processes after glucose loading could not make themselves valid the standing potential remains low and does not show the same increase as in the normal subjects. It is namely known that the relation between NAD, NADH, and NADPH, NADP is diminished in diabetes due to a relative increase in NADH and a relative decrease in NADPH.

(3) The permeability of the capillary membrane is increased due to the storage of collagen glycoprotein with a large content of hydroxyproline.

The decrease in the LP/DT ratio during glucose loading in the control group is only occasional in diabetics however significant. This decrease is probably a specific symptom for the diabetic retinopathy. It may be that in diabetics secondary metabolic processes even get worse during the loading.

Considering the known changes of semipermeable membranes and the results mentioned here it may be possible to determine the quality of the permeability of these membranes by means of the EOG. Perhaps it may be possible to check their function during the course of the disease.

We surely do not assert that a lowered LP/DT ratio is always the result of the above mentioned processes. Other causes for a lowered ratio may be a lowered activity of the receptors, a lowered circulation in the choriocapillaris and a lowered electrical resistance between the retina and the choriocapillaris resulting in an inability to retain a potential difference.

Summary

The light peak dark trough ratio of the EOG has been examined in a group of normal subjects and in a group of diabetic patients before and after intravenous glucose loading. In the normal group this ratio appeared to be significantly higher after the loading than before. In the diabetic group no significant increase could be observed. In the discussion an attempt is made to explain this difference between the normal subject and the diabetic patient.

Table III
Effect of antiglaucomatous treatment on the thickness of the corneal stroma
in normal eyes

			Before treatment		After treatment		ΔT (μ)
			IOP (mm Hg)	T (μ)	IOP (mm Hg)	T (μ)	
EO	m	os	14	466	12	440	4
HB	f	os	17	466	12	464	- 2
FK	m	os	12	472	10	448	0
IS	m	os	15	434	13	432	- 2
LB	m	od	13	440	10	480	10
MB	f	os	16	450	12	446	- 4
GK	f	os	18	450	14	426	- 4
Ik	m	os	18	490	14	490	0
IS	f	od	16	408	13	408	0
mean			15	454 \pm 9	12	434 \pm 9	1 \pm 2

The table shows corresponding values of IOP and thickness of corneal stroma in normal eyes before and after treatment for 2 days with pilocarpine acetazolamide and adrenaline. Lower line mean \pm standard error of mean.

Results

Table I shows data for 8 patients in whom both eyes fulfil the criteria outlined above. In 3 cases the corneal stroma was found to be thicker in the eye with elevated IOP, in 4 cases it was thinner, and in one case no difference was found. The mean value of the differences (0.004 mm) is found not to differ statistically significant from zero ($P < 0.4$).

Table II shows data for 14 patients with initial IOP in one eye above 30 mm Hg and a fall to between 10 and 20 mm Hg after treatment. The mean value of the thickness differences is found to differ statistically significant from zero ($t = 5.15$, $P < 0.001$).

The effect of the given treatment upon the thickness of the stroma has been studied by giving the same treatment to a group of volunteers (Table III). A small reduction in IOP was seen and no effect upon thickness. In 4 cases the thickness was smaller after the treatment, in 3 cases it was greater, and in 2 cases identical values were found before and after treatment for 48 hours. The mean of the differences is found not to differ statistically significant from zero ($P < 0.6$).

References

- 1 Arden G B Barrada A & Kelsey J H New clinical test of retinal function based upon the standing potential of the eye *Brit J Ophthalm* 46 449-467 1967
- 2 Arden G B & Barrada A Analysis of the electro oculograms of normal subjects *Brit J Ophthalm* 46 465-480 1962
- 3 Caird F I Pirie A & Ramsell T G Diabetes and the Eye Blackwell Oxford 1969
- 4 Urbanova S Vliv podane glukozy na elektrookulogram *Cs Oftal* 9: 75-18 1969
- 5 Henkes H E van Lith G H H Gassner P D & de Haas J P Electrodiagnostic procedures in diabetes. In The clinical value of electroretinography Vth ISCERG Symp Ghent, 393-402 1966 Karger Basel/New York 1968
- 6 Aris E C Electro oculographic predictors of diabetic retinopathy In Retinal degeneration: ERG and optic pathways Proc IVth Symp ISCERG 1965 Jap J Ophthalm Vol 10 Suppl Tokyo 1966 pp 128-129
- 7 Voell W C Azide sensitive potential difference across the eyebulb *Amer J Physiol* 110 217-238 1957

Discussion

A direct parallel to the previous study on reduced IOP (Ehlers & Riise 1961) would be a report on a greater number of patients with unilateral non irritative (simple) glaucoma in one eye and a normal contralateral eye. These patients are unfortunately seen only seldom. Table I includes but 8 patients. No significant difference in thickness has been found. Sbordone (1953) studied the corneal thickness in acute and chronic glaucoma. In two cases of acute glaucoma the thickness was increased considerably—an observation made several times during the present study. In 12 cases of long lasting pressure difference (chronic glaucoma) the cornea of the eye with the higher pressure was thinner in 9 cases and thicker in 3 cases. On an average the cornea was thinner in the eye with the higher pressure. Ytteborg & Dohlman (1964) presented a rather impressive table including 15 cases of IOP of 31 to 68 mm Hg in one eye and normal IOP in the other eye. No epithelial oedema was present. A comparison of the two mean values showed no significant difference in thickness ($P < 0.20$) however by paired comparison a value of $P < 0.02$ is found suggesting an increased thickness of the total cornea at increased IOP. From studies on the physiology of the cornea (Maurice & Giardina 1951, Honegger 1962) it is evident that when the endothelial barrier is removed or broken down an increase in stromal thickness occurs. This is probably what happens in acute glaucomas and after operations where considerably increased thickness is found. However it says nothing about the effect of IOP when an intact endothelium is present. In the above mentioned table of Ytteborg & Dohlman it is not mentioned whether all cases were non irritative glaucomas neither is it mentioned whether the pressure in any of the contralateral eyes had been reduced by operation. Iuglio (1967) studied 5 cases at high normal and low IOP. The cases are not further characterized and for the reasons mentioned above several interpretations are possible.

By comparing the thickness of the stroma of the same cornea at normal and high IOP the data in Table II were found. The thickness increased significantly ($P < 0.001$) when the IOP was reduced from above 30 mm Hg to the normal range ($10 \leq \text{IOP} \leq 20$). The treatment employed to reduce the IOP had no measurable effect upon the thickness (Table III). It therefore appears that the changes in thickness are caused by the changes in IOP. The IOP had probably been elevated for a prolonged period of time as no treatment were given the two foregoing days. The values at normal IOP were not measured until the pressure had been normalized for 1 or 2 days. The uncertainty of not being in a steady state condition when measuring pressure and thickness is therefore probably eliminated. It may be concluded that the IOP exerts a reducing effect upon the thickness. This agrees with the mentioned *in vitro* experiments on monkey eyes and supports the existence within the physiologic range of me-

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MESODERMAL DYSGENESIS OF THE CORNEA AND IRIS (RIEGER'S ANOMALY)

Report of a Case

BY

BIRGITTA ZETTERSTRÖM

Mesodermal dysgenesis of the cornea and iris is a developmental anomaly which occurs as early as the seventh month of intra uterine life. A hereditary tendency is well established and a vast literature on the condition exists. *Herwig* *Rieger* (1934-1935) studied the anomaly extensively and described the clinical features in more detail. It is now generally known as Rieger's anomaly. He observed the association of dental anomalies in some cases and later assumed that dental anomalies and the dysgenesis could be connected.

The characteristic features of the condition are abnormality in the development of the cornea, the angle of the anterior chamber and the anterior stromal layer of the iris whilst the sphincter pupillae and the posterior mesodermal layer of the iris are normally developed. Mesodermal remnants span the chamber angle and this may give rise to buphthalmos or infantile glaucoma. Anterior synechiae from the iris to the posterior aspect of the corneal periphery may lead to traction on the pupil producing corectopia, dyscoria or slit-like pupils.

Sharf (1941) described 2 cases in which progressive iris atrophy caused a tear in the iris and resulted in glaucoma.

The clinical course of mesodermal dysgenesis of the cornea and iris is still obscure. Few workers have discussed it (*Starke* 1951, *Kittel* 1956), *Lemmington*

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chanical factors in the maintenance of normal corneal thickness and state of hydration

Summary

The thickness of the corneal stroma has been studied in cases of glaucoma. In 8 cases of unilateral glaucoma no difference in thickness could be observed. In 14 cases of glaucoma a statistically significant increase in thickness was observed when the intraocular pressure was reduced by medical treatment from above 30 mm Hg to the range 10-20 mm Hg. In a control series the treatment had no effect upon the thickness. It is concluded that within the physiologic range increased pressure reduces the thickness of the cornea.

References

- Ehlers N (1966) The fibrillary texture and the hydration of the cornea. - *Acta ophthalmol* 44 620-630
- Ehlers N (1967) Mechanical factors in the maintenance of normal corneal deturgescence. - *Acta ophthalmol* 45 658-672
- Ehlers N & Riise D (1967) On corneal thickness and intraocular pressure. - *Acta ophthalmol* 45 809-813
- Honegger H (1962) Quantitative Untersuchungen über die Hornhautendothelregeneration in vivo. - *Graefes Arch Ophthalmol* 165 31-42
- Honegger H & Gence E (1968) Hornhautdickenmessung. Ein Vergleich verschiedener Geräte. - *Graefes Arch klin exp Ophthalmol* 174 262-270
- Iuglio V (1967) Influenza della pressione intraoculare sullo spessore della cornea umana. - *Boll Soc ital Biol sper* 43 1904-1905
- Maurice D M & Giardini A A (1951) Swelling of the cornea in vivo after destruction of its limiting layers. - *Brit J Ophthalmol* 35 191-197
- Sbordone G (1953) Ricerche sullo spessore della cornea in occhi glaucomatosi. - *Rass Ital Ottal* 22 262-268
- Ytteborg J & Dohlman C H (1965) Corneal edem and intraocular pressure. II. Clinical results. - *Arch Ophthalmol* Chicago 74 471-484

& Rieth (1958) considered progressive iris atrophy giving rise to partial anidria to be of great pathological significance. The literature however does not contain any case to the best of the author's knowledge in which the anomaly was diagnosed early and the clinical course was followed up for a prolonged period of time.

A case of mesodermal dysgenesis of the cornea and iris was seen in this Department in which the anomaly was suspected in the first week of life its presence being confirmed in the seventh month and the clinical course has been followed up for four years at the time of writing. This was therefore considered to be sufficiently interesting to be reported.

Case Report

The patient was a first child. Her weight and height at birth were 3550 g and 50 cm respectively. Her mother aged 32 years had been healthy throughout her pregnancy and was delivered in the fortieth week. The patient's father had the same eye disease as she herself otherwise the family history was irrelevant.

Immediately after the birth of the patient both corneae were found to be so opaque that it was impossible to inspect the anterior chambers. The cornea was found to blend with the sclera without sharp demarcation at the limbus and a large number of superficial vessels were present in this area. Both eyes were white and the cornea did not stain with fluorescein. There was no appreciable response to light and the intra-ocular pressure was normal.

The patient was referred to the Paediatric Unit of this hospital for further investigation. The Gonococcal complement fixation test was negative as was Rubella culture. The toxoplasma dye test and the complement fixation test showed $-1/10$ and $-1/7$ respectively. The test for *Listeria* was negative. The values of serum calcium and alkaline phosphatase were normal. Amino acid analysis by paperchromatography revealed no abnormality. The blood count was normal the Wasserman reaction was negative and there was no evidence of systemic disease.

During the first few weeks after birth the corneal opacity of both eyes gradually receded. The intra-ocular pressure was normal being $8\frac{1}{2}$ (12 mm) as measured under anaesthesia with a Schiötz tonometer and Goldmann's applanation tonometer for both eyes.

At the age of eight months both corneae had become sufficiently translucent to enable some details of the anterior chambers of both eyes to be recognized. As had been found at birth the cornea blended with the sclera without any sharp demarcation and there was marked vascularisation of the limbus. The pupil margins were only partly visible but the colour of the iris which was bluish grey could be distinguished. Fiform bands were visible extending from the anterior lamina of the iris to be inserted into the posterior surface of the cornea. The corneal opacities however had not yet receded sufficiently for the fundus to be inspected. The intra-ocular pressure of both eyes was 12 mm as measured with Goldmann's applanation tonometer.

Some details of the anterior chamber which appeared to be malformed were now sufficiently clearly visible to be photographed (Fig. 1).

At the age of twenty months both corneae had become still more translucent. The demarcation between the cornea and sclera was still indistinct and numerous blood vessels resembling superficial vessels in type were still present in this area. The

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MALIGNANT MELANOMAS OF THE HUMAN UVEA

Recent Follow up of Cases in Denmark 1943-1952

BY

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All cases of intra ocular malignant melanomas in Denmark within the ten year period 1943-1952 were personally investigated clinically histopathologically and prognostically and the results published in a monograph in 1963 (14)

The present follow up includes the same cases the observation period now having been extended by a further five years

Material and Methods

As regards collection analysis and the clinical and histopathological aspects of the material reference is made to the above mentioned monograph (14) Each case has now been followed until death or up to the terminal date of the follow up January 1 1966 The shortest observation period has therefore been 13 years and the longest 23 years This was made practicable by the aid of general practitioners the census registers the Danish Cancer Registry the Central Card Index for Deaths of the Danish Health Department and the National Record Office where all death certificates are

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Fig 1
The patient's eyes at the age of eight months

entire pupil margin was now visible. The intra ocular pressure of both eyes was 14 mm (Fig 2)

At the age of three years and two months the demarcation between the cornea and sclera was more clearly visible and the limbus was found to be less vascular than at the previous examination. The pupil was clearly seen. The iris which showed markedly atrophic changes in places was clearly outlined. Filiform and chord like membranes were seen to stretch from the periphery of the anterior lamina of the iris across the anterior chamber to find insertion into Descemet's membrane. The visual acuity of both eyes was 5/20. The cornea was 9.5×10 mm in diameter. The intra u ular pressure was 14 mm (Fig 3)

At the age of four years the visual acuity was found to be 2/10 for both eyes. Retinoscopy showed the refraction of both eyes to be +4.00. The fundi could not be clearly distinguished but appeared to be normal. The intra ocular pressure was 19 mm (Fig 4)

The number of teeth corresponded to the age of the infant

The gonioscopic appearances was indistinct. In places membranous bands were seen to span the angle chamber extending from the anterior lamina of the iris to the poste



Fig 2
The patient's eyes at the age of twenty months

filed as well as by hospital records and post mortem reports. Where autopsy had been performed all available histological material was procured and examined.

In this work surviving patients were not examined personally except for a few cases in the Ophthalmic Tumour Centre at the Ophthalmic Pathology Laboratory, the status of the patients being based on the hospital records and on information from general and ophthalmic practitioners.

Some borderline cases were re-evaluated with respect to cell type, reticulin content and pigment content which explains small differences of the figures in some tables compared with the same tables of the previous publication.

The data collected were analysed by the K-H system (14). The distributions were compared using the χ^2 test.

The table numbers in squared brackets refer to tables in the previous publication (14) for the sake of comparison. Table numbers and numbers in parentheses refer to the present publication.

Results

A survey of the follow up can be seen in Table 1 [Table 39]. The same number of patients as previously could be traced so that a follow up percentage of 99 was obtained. 72 per cent of the total number being dead at the time of follow up. Further reference to the single groups in Table 1 will be made below. The cases of iris melanoma will be dealt with separately at the end.

Follow-up of survivors (Choroid and ciliary body tumours) (see Table 1). Regarding the two patients alive with previous orbital recurrence reference is made to Table 2 below (case Nos. 260 and 266). These patients are the same as those in [Table 39].

The patient alive with metastasis (case No. 231) showed signs of this 13 years after enucleation. The primary tumour of the mixed cell type had invaded the sclera slightly. By explorative laparotomy a melanoma metastasis in the omentum was found and totally extirpated. The patient was healthy at the time of follow up but died later with metastases present. The two patients alive with signs of metastases in the previous table [Table 39] died shortly after the previous follow up.

Follow up of dead (Choroid and ciliary body tumours)

From Table 1 it can be seen that half of the 214 dead patients died in hospital and half at home. Of the latter about half had been in hospital shortly before death. In 154 of the cases (53 per cent) the patients died with metastases present. In about two fifths (38.5 per cent) of these the metastases were verified by autopsy or premortal biopsy and in a further 6 per cent by explorative laparotomy without histological verification. The rest died with metastases present according to death certificate. The overall autopsy frequency of the material was 31 per cent.



Fig 3

The patient's eyes at the age of three years and two months. Visual acuity was bilaterally >20



Fig 4

The patient's eyes at the age of four years. Visual acuity was bilaterally >10

rior aspect of the cornea. Fine details could not be distinguished. The angle of the chamber was open and of average width.

The eyes of the infant's father, aged 37 years, were examined and photographed (Fig 5). Demarcation between the cornea and sclera was indistinct and fibres were seen to extend from the iris in Descemet's membrane in places. The lenses were clear and the fundi did not show any abnormality. The corneae were 10×10 mm in diameter. The visual acuity of the right eye was 0.2 ($+7.00$), that of the left being 0.4 ($+7.5$). The intra-ocular pressures were 8/5.5 Schiotz. There was no evidence of dental anomalies.

The maternal and paternal grandparents as well as their brothers and sisters and the children of the latter had no known eye disease.

The patient's father stated that his sight had improved since childhood. As he had not been ophthalmologically examined until adult age, objective infor-

Table 1
Survey of follow up

	Chor	Cil body	Chor + cil body		Iris	Uvea	
	Number	Number	Number	%	Number	Number	%
Followed up	281	11	292	99	10	302	99
Not followed up	3	-	3	1	-	3	1
Alive no signs of metast	71	4	75		7	82	
Alive w excised orbital recur	2	-	2		-	2	
Alive w signs of metast	1	-	1		-	1	
Total alive	74	4	78	27	7	85	98
Died at home	107	1	108		1	109	
Died in hospital	104	2	106		2	108	
Total dead	211	3	214	73	3	217	72

Orbital recurrence

A survey of these cases can be seen in Table 2 [Table 43]. Intra ocular biopsy was performed in 12 cases of the whole series. Among these were one case of orbital recurrence, two of latent tumour cells (16) and one case of benign post operative conjunctival melanosis.

In the rest of the material of choroidal and ciliary body melanomas without biopsy (780 cases) seven cases of orbital recurrence were found i.e. 2.5 per cent. No new local recurrence had come to light since the previous record. One patient (case No 743) with a recurrence of latent tumour cells in the orbit 24 months after enucleation had died from other cause 12 years after enucleation without further local recurrence or metastases. The orbital recurrence appeared in the present series at an average of 2 years after the primary operation.

Regarding therapy of the local recurrence in the present series exenteration of the orbit was performed in two cases, excision of the recurrence in five. In two of these a second recurrence required orbital exenteration. The two patients with latent tumour cells had their recurrences excised. Both had died 3 years



Fig 3

The eyes of the patient's father aged 31 years Visual acuity of the right eye was 0.2 that of the left being 0.4

mation about this point was lacking Fig 5 shows the eyes of the patient's father

This case is of special interest inasmuch as the clinical course of the anomaly has been followed up for four years at the time of writing There was photographic evidence of regression of the opacity of the cornea concurrently the pathological changes in the anterior chamber became visible and there was objective evidence of improvement of vision

Summary

A case of mesodermal dysgenesis of the cornea and iris is reported in which the anomaly was suspected in the first week of life its presence being confirmed in the seventh month and the clinical course of the condition has been followed up for four years at the time of writing

Interesting features of the case were that the bilateral congenital opacity cleared sufficiently for details of the anterior chamber to be photographed and that there was objective evidence of improvement of vision

References

- Küttel V (1956) *Klin Mbl Augenheilkd* 129 464
- Lemmington W & Riethe P (1958) *Klin Mbl Augenheilkd* 135 377
- Rieger H (1934) *Zeitschrift für Augenheilkunde* 53 98
- Rieger H (1935) *Gräefes Arch Ophthalm* 133 602
- Scharf J (1941) *Klin Mbl Augenheilkd* 106 411
- Starke H (1951) *Gräefes Arch Ophthalm* 151 384

Table 2
Survey of cases with orbital recurrence in the present series

Case No	Duration of first attack	Primary operation	Intraocular biopsy	Size (mm) of primary tumor	Local invasion	Extracranial extension	Invasion of optic disc	Invasion of optic nerve	Cell type of primary tumor	Pathologic picture	Local recurrence	Survival
6	1 mths	Encl	-	60	+	+	-	-	Mixed predom. spindle II	Absent	10 mths	-
15	36 mths	Enucl + partial exent of orbit	-	Diffuse uveal growth	+	+	-	+	Mixed predom. epith	Mixed	4.5 mth	-
113	18 mths	Encl	-	32	+	-	-	-	Mixed equally spindle and p	?	14 mths	-
1	11 days	Enucl	-	?	?	?	?	?	?	?	6 yrs.	8-9 yrs.
133	8 days	Encl	-	91	+	+	+	-	Epith	Absent	5-6 yrs	6 yrs.
215	0 yrs? 2 mths?	Enucl	-	132	+	+	+	-	Mixed equally spindle and p	Light	9 mths	-
243	1 mth	Enucl	Prooperatively	90	+	-	-	-	Spindle B	Light	4 mths	-
58	4 mths	Enucl	Prooperatively	?	?	?	?	?	Mixed	?	18 mths	-
60	18 days	Enucl	2 days before op	40	-	-	-	-	Spindle II	Moderate	6 yrs	-
66	1 mth	Enucl		?	+	-	+	-	Epith	?	8 mths	-

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ON CORNEAL THICKNESS AND INTRAOCULAR PRESSURE II

*A clinical study on the thickness of the corneal
stroma in glaucomatous eyes*

BY

NIELS EHLERS

In a previous study (Ehlers & Riise 1967) it was demonstrated in a group of patients with unilateral retinal detachment that when the intraocular pressure (IOP) was low the corneal thickness was greater than in the contralateral normotensive eye. This observation was in agreement with *in vitro* experiments on monkey eyes (Ehlers 1966, 1967) showing that the IOP exerts a reducing effect on the swelling of the cornea. The *in vitro* experiments further suggested that a reduced thickness of the corneal stroma should be found in eyes with elevated IOP.

Only few reports on the correlation between corneal thickness and increased IOP exist (Shordon 1953, Ytteborg & Dohlman 1965, Iuglio 1961) and the results are contradictory.

The purpose of the present study has been to compare values for the thickness of the corneal stroma in eyes with high IOP with 1) the thickness of the stroma in the contralateral normotensive eyes and 2) the thickness of the stroma in the same eyes after the IOP has been normalized by medical treatment.

Methods

Patient material All patients included in this study suffered from non operated glaucoma, had good central vision and clinically normal corneas, especially no epithelial oedema. Patients admitted to the Eye Department for glaucoma were

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Table 2 (cont)

[illegible]

informed not to treat the glaucoma on the day of admission and the day before. As a result a number of patients showed elevated IOP. The thickness of the corneal stroma was measured and compared with the thickness in the contralateral eye if this showed normal IOP (Table I) and with the thickness in the same eye after the IOP had been reduced by treatment with pilocarpine, acetazolamide and in some cases adrenaline if the contralateral eye could not be used for comparison (Table II). In order to rule out an effect of the given medical treatment on the thickness of the corneal stroma a control group of persons with normal IOP was included (Table III).

Measuring technique The corneal thickness was measured according to the principle of Jaeger using the attachment I to the Haag Streiff slit lamp. This apparatus appears to be the most reliable at the present time (Honegger & Genee 1968). The procedure followed has previously been reported (Ehlers & Riise 1967). Although cases showing epithelial oedema have been excluded, a subclinical oedema might increase epithelial thickness. For this reason only the stromal thickness was measured as illustrated in Fig. 1.

The results have been statistically evaluated by paired comparison using the *t* test as corneal thickness was found not to differ statistically significant from the normal distribution (Kriese Hansen to be published). In tables II and III only one eye from each patient has been included in order to have statistically independent data.

Table I
Corneal thickness in cases of unilateral glaucoma

		Glaucomatous eye		Contralateral eye		ΔT (μ)
		IOP (mm Hg)	T (μ)	IOP (mm Hg)	T (μ)	
KH	f	60	488	21	484	-4
EL	m	32	478	17	478	0
MJ	f	38	480	20	492	12
EM	f	70	426	17	444	18
KF	m	38	440	16	436	-4
CM	f	32	410	10	398	-12
AT	f	62	458	10	464	6
TJ	f	50	460	16	476	16
mean		48	455 \pm 10	16	459 \pm 11	4 \pm 4

The table shows corresponding and simultaneous values of IOP and thickness of corneal stroma in patients with unilateral glaucoma. Lower line: mean \pm standard error of mean.

Table 2
Survey of cases with orbital recurrence in the present series

Cum No	Dur of past hist	Primary operation	Intraocular biopsy	Size (mm) of primary tum	Scleral invasion	Ext scleral extensions	Involvement of optic disc	Involvement of optic nerve	Cell type of primary tum	Follow up (months)	Local recurrence	Survival
6	1 mths	Enucl	-	60	+	+	-	-	Mixed pred n spindle B	Absent	10 mths	-
6	6 mth	Enucl + partial ext of orbit	-	Diffuse uveal growth	+	+	-	+	Mixed pred m ph	Marked	4-5 mths	-
116	18 mths	Enucl	-	52	+	-	-	-	Mixed equally spindle and ep	?	14 mth	-
17	11 days	Enucl	-	?	?	?	?	?	?	?	6 yrs	8-9 yrs
185	8 days	Enucl	-	1	+	+	+	-	Epith	Absent	5-6 yrs	6 yrs
15	0 yrs. 2 mths	Enucl	-	132	+	+	+	-	Mixed equally spindle and epith	Lght	9 mths	-
243	1 mth	Enucl	Prep r at cly	90	+	-	-	-	Spindle B	Lght	4 mths	-
58	4 mth	Enucl	Oper at cly	?	?	?	?	?	Mixed	?	18 mths	-
60	10 days	Enucl	2 days before op	40	-	-	-	-	Spindle B	Mixed m	6 yrs	-
66	1 mth	Enucl	-	?	+	-	+	-	Epith	?	8 mths	-

Table 11
Effect of reduction of elevated IOP upon thickness of corneal stroma

			Before treatment		After treatment		ΔT (μ)
			IOP (mm Hg)	T (μ)	IOP (mm Hg)	T (μ)	
ND	m	os	56	446	29	432	36
OS	m	■	48	404	19	434	30
VJ	f	os	43	426	18	460	34
AT	f	os	69	458	12	500	42
PH	m	od	44	432	15	438	6
HK	m	od	38	448	18	450	32
AV	m	od	32	459	17	452	0
VN	f	od	37	448	19	478	30
AP	f	■	39	464	16	468	4
HS	m	od	35	454	20	466	12
AM	m	od	32	438	17	472	34
EJ	f	os	34	458	20	468	10
TP	m	od	35	496	12	436	10
MC	f	os	30	434	20	438	4
mean			49	442 ± 4	18	462 ± 5	20 ± 4

The table shows corresponding values of IOP and thickness of corneal stroma in eyes in high (IOP \geq 30 mmHg) and normal ($20 \geq$ IOP \geq 10 mmHg) intraocular pressure. The pressure was reduced by treatment with pilocarpine, acetazolamide and adrenaline. Lower line mean \pm standard error of mean.



Fig 1

In the corneal microscope the endothelium appears single contoured. The epithelium however shows a definite thickness and it is therefore possible to measure total thickness (a) or as in the present study only stromal thickness (b).

Table 2 (cont)

1	2	3	4	5	6	7	8	9	10
Cell type	Cell type	Cell type	Cell type	Cell type	Cell type	Cell type	Cell type	Cell type	Cell type
Exm of arb	Ep th			16 mths	6 mths		23 mths	1 mth	D th rt
E na f b	M d, p dom ep h		11 y				12 mths	3 mth	D th rt
λ y				14 mth	At th m t m		0 mths	6 mths	D th rt
E t r p Ex na forb.	M d, quality p d p h	M d, p d m p th		10 yrs	14 yrs 18 mths	M d, p d m, p d l A	10 y	4-5 yrs	12 mth
1X Ex t of b	Ep h			9 y	124 mths 121 mths		9 y	6 mth	2 yrs
X ray							14 mth	4 mth	D th rt
Es p	Lai t p d l B		10 y				12 y	10 yrs	D th rt
Esu p	Lai t m d p d m p h		Absent	34 mth	15 mth		3 yrs	18 mths	A t pay
E t r p	M d		Absent	15 y					
Ca rp			15 yrs						

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DENDRITIC (HERPETIC) KERATITIS

1 Incidence – Seasonal Variations – Recurrence Rate – Visual Impairment – Therapy

BY

M S NORN

Herpetic keratitis is a frequent disease often causing lost working days. The disease represents a steadily increasing problem within our highly advanced social system where other diseases are combated with greater success.

The present possibility of instituting rational treatment with 5-iodo-2-deoxyuridine (IDU) which interferes directly with the viral metabolism is regarded as a great improvement.

Numerous reports have been published on this subject since Kaufman *et al* (1967) introduced IDU treatment against dendritic keratitis. A favourable result has been noticed in most cases (Kaufman, Anseth *et al*, Capperucci, Mach *et al*, Laibson *et al*, Maxwell, Patterson *et al*, Sood *et al* etc.).

The response to IDU has been studied through double-blind trials using as placebo water or substances of at least doubtful therapeutic value.

These trials have shown IDU to give more rapid cure than placebo (Patterson, Laibson, Jepson, Hart *et al*, Davidson, Burns).

Ey *et al* and Marken *et al* took up a more reserved attitude. The latter found carbolic acid to have a better effect than IDU. Gilkes found no significant difference between the effects of iodine cauterisation and IDU therapy.

Some workers state that a favourable response to IDU is only obtainable

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Fankhauser F, Lotmar W & Foulter A Photocoagulation Through the Goldmann Contact Glass II An Apparatus Using a Quasi Continuous Laser Source AMA Arch Ophthalmol 79 674 1969

Fankhauser F, Lotmar W & Foulter A Photocoagulation Through the Goldmann Contact Glass III Clinical Experience With an Apparatus Using a Quasi Continuous Laser Source AMA Arch Ophthalmol 79 684 1968

Fankhauser F & Lotmar W Methods of Photocoagulation Through the Goldmann Contact Glass Mod Probl Ophthalm vol 7 pp 256 212 (Karger Basel/New York 1969)

Linder B Acute Posterior Vitreous Detachment and Its Retinal Complications Acta Ophthalm (Abh) Supplementum 87 (Munksgaard Copenhagen 1966)

and 12 years respectively after the enucleation or 18 months and 10 years after the recurrence

Disregarding the last mentioned two cases death occurred at an average of 19 months after the orbital recurrence or about 4 years after enucleation

Prognosis

This is estimated on various clinical and histopathological features in a group of 230 cases each followed up 15 years after the enucleation

The prognosis in relation to sex and age can be seen in Table 3 [Table 49] As was previously found the prognosis for men is independent of age whereas women below the age of 40 seem to have a better prognosis than women above that age

The prognosis in relation to size is recorded in Table 4 [Table 52] A com

Table 3
Prognosis in relation to sex and age (15 year obs period)

Age	Males				Females			
	Alive	Dead		Total	Alive	Dead		Total
		metast	other cause			metast	other cause	
0-9	1	-	-	1	-	-	-	-
10-19	1	-	-	1	-	-	-	-
20-29	-	1	-	1	3	1	-	4
30-39	10	4	-	14	5	1	2	8
40-49	12	16	-	28	7	12	1	20
50-59	11	21	1	33	11	20	3	29
60-69	7	20	12	39	7	10	3	20
70-79	2	7	7	16	-	5	6	11
80-89	-	-	-	-	-	3	2	5
Total	44 33 %	69 52 %	20 15 %	133 100 %	28 29 %	52 54 %	17 17 %	97 100 %
	5 % < p				0.1 % < p < 1 % for < 40 yrs			

(Testing based on the age groups < 40 yrs 40-60 yrs and > 60 yrs The groups of alive and died from other cause have been combined)

haemorrhages Profuse retinal haemorrhages have been observed only in a few cases (Dow 1965 Quock & Donohoe 1967)

Since the introduction of a clinically applicable method of fluorescence angiography (Novotny & Alvis 1961) this procedure has been widely used for investigation of the retinal and choroidal circulations (Shikano & Shimizu 1968 Wesing 1968, Rosen 1969) In Eales disease leakage of fluorescein from the diseased vein has been consistently observed According to Shikano & Shimizu the fluorescein pattern is due to factors such as diffuse leakage of dye from arterioles and capillaries resulting in the formation of multiple irregular fluorescent spots and retention of dye in the affected vein wall

The present paper describes the appearance of retinal vascular lesions as revealed by fluorescence angiography in a case of sarcoidosis

Method

With the patient in a sitting posture the pupil is dilated with Mydracyl® (Alcon Lab) and a 10 per cent solution of sodium fluorescein is injected into an ante cubital vein

The Zeiss fundus camera equipped with an automatic film changer (Robot motor recorder) is used The fluorescence excitation filter is a blue filter (Schott BG 12) which is placed in front of the xenon flash tube The barrier filter (Schott GG 14) is placed in front of the film This filter transmits light of wave lengths of about 490 nm and longer: ≈ 15 per cent of the light is transmitted at 490 nm and 85 per cent at 530 nm The power source for the xenon flash tube is the Zeiss Siemens flash generator

Case Report

The patient is a woman aged 35 years had several episodes of otitis in childhood but otherwise had enjoyed good health until she developed pain in the lower half of the thorax She was admitted to the Lung Clinic St Gorans Hospital Stockholm where the diagnosis of sarcoidosis (uveo parotid fever) was made

X ray of the lungs disclosed bilateral hilar lymphadenopathy and at a later stage a fine disseminated mottling in the parenchyma Both parotid glands were enlarged but there was no evidence of sialolithiasis or septic parotitis

A few weeks after her admission ophthalmological examination revealed anterior uveitis in the left eye and two months later in the right After a further four weeks the bilateral anterior uveitis was found to have progressed and there was evidence of involvement of both fundi Concurrently the patient developed a peripheral facial paralysis on the left side (Bell's palsy) and mild lagophthalmos as a sequel About six

Table 4
Prognosis in relation to size (15 year obs period)

mm ²	Alive	%	Dead (metast)	%	Dead (other cause)	%	Total	%
< 100	53	40	55	42	24	18	132	100
> 100	16	20	31	60	12	15	49	100
Not determinable	3		15		1		19	
Total	72		101		37		210	

0.1% < p < 1% (In testing the groups of alive and died from other cause have been combined)

parison has been drawn between patients with primary tumours of 100 mm² or less and tumours exceeding 100 mm² at the time of enucleation. Measurement in only two dimensions was possible in the present series. The analysis shows that the prognosis is significantly worse in cases of tumours with an area of more than 100 mm². No significant difference was found in using any other groupings. The prognosis in relation to scleral invasion and extrascleral extension can be seen in Table 5 [Table 53].

In both cases the prognosis appears to be worse when invasion and especially extrascleral extension was found in the enucleated eyeball. In cases of invasion of the optic disc, the optic nerve and the retina, no significant increased lethality was found.

The prognosis in relation to cell type can be seen in Table 6 [Table 54]. The classification of the tumours is according to Callender (7). The table also records the prognosis in the whole series. It can be seen that 53 per cent had died with metastases present over a 15 year observation period and that the lethality of the epithelioid group is two and a half times as high as in the spindle B group. It can also be seen that after revision only a few tumours in our series could be classified as spindle A or fascicular.

Fig. 1 illustrates the actuarial survival curves for melanoma cases of the different cell types. In these curves the spindle types are grouped together and the few fascicular cases left out. It can be seen that spindle cell tumours yield an 80 per cent chance of survival five years after enucleation, whereas only about 30 per cent of patients with the epithelioid type have a chance of survival. The malignancy of the epithelioid tumours is also illustrated by the fact that more than half the patients with this tumour die with metastases present within

months later the anterior uveitis was found to have regressed. During that time the patient had a short episode of dizziness which was accompanied by a tendency to fall to the left.

Laboratory findings: The sedimentation rate ranged between 10 and 15 mm/hour. The blood count was normal and routine urinalysis did not reveal any abnormality. The Mantoux test was positive but direct microscopy, guinea pig inoculation and culture in Lowenstein-Jensen medium failed to reveal tubercle bacilli in the sputum and gastric juice. Serum calcium was 10.6 mg%, the urinary calcium level was 17.4 mg%, this corresponded to a urinary calcium output of 0.3 g per twenty-four hours. Liver tests, sternal puncture, retromandibular biopsy of a lymphatic gland, the toxoplasma dye test and the complement fixation test were negative. The Heim test was positive.

The patient was given prednisolone per os. Initially she received a dose of 10 mg \times 4 per day. This dose was gradually reduced to 5 mg \times 2 daily but was again increased if required. Eye drops of mydriatics and corticosteroid preparations were used.

Ocular manifestations: There was mild bilateral anterior uveitis with slight ciliary injection and aqueous flare. Cells were present in the anterior chamber and there were multiple keratic precipitates on the corneal endothelium. There were no posterior synechiae but there was evidence of inflammatory deposits in the chamber angle. An inflammatory reaction in the vitreous body occurred on several occasions.

Two months after the diagnosis of iridocyclitis had been made both fundi showed disseminated haemorrhages and multiple perivascular lesions. In the right fundus small fresh haemorrhages involved the areas above the optic disc and between its main ascending branches of the blood vessels; some of these haemorrhages became confluent and associated exudates appeared (Fig. 1A). Smaller haemorrhages involved the left fundus.

Both the retinal arterioles and venules showed changes. In the upper part of the right fundus the haemorrhages were soon absorbed. Where this had occurred a vein branch was seen to be occluded. At ophthalmoscopy an arteriole running adjacent to the latter appeared to be almost completely occluded (Fig. 1B). Newly formed blood vessels originated from the occluded vessels forming a fan-like pattern in the retina. Several dilated and tortuous branches of the venules joined and opened into a main branch. In other areas a few small exudates and haemorrhages adjacent to the arterioles were present.

There were numerous phlebotic lesions (Fig. 2). These included segmental sheathing and thickening of the vessel wall in places. The blood column of some vessels was considerably narrowed, that of others being not visible at all. Perivascular exudates were seen.

About one year after the appearance of the ocular symptoms the patient developed bilateral secondary glaucoma and oedema of the right optic disc. The iridocyclitis and the changes in the chest persisted.

Findings at fluorescence angiography: In the arterial phase the arterioles were clearly outlined as far as the occluded portion of the vessels in the right fundus.

Table 5

Prognosis in relation to scleral invasion and extrascleral extension (15 year obs period)

	Alive	%	Dead (metast)	%	Dead (other cause)	%	Total	%	p
- scleral inv	32	32	46	45	23	23	101	100	$1\% < p < 5\%$
+ scleral inv	22	18	76	63	23	19	121	100	
- extrascl extension	51	28	92	51	38	21	181	100	$0.1\% < p < 1\%$
+ extrascl extension	3	7	30	73	8	20	41	100	

(In testing the groups of alive and died from other cause have been combined)

Table 6

Prognosis in relation to cell type (15 year obs period)

Cell type	Alive		Dead (metast)		Dead (other cause)		Total	
	Number	%	Number	%	Number	%	Number	%
Spindle A	6		1		2		9	
Spindle B	39	53	24	52	11	15	74	100
Mixed	23	21	69	62	19	17	111	100
Epithelioid	2	8	21	81	3	11	26	100
Fascicular	2		4		2		8	
Not determined								
Total	72	31	121	53	37	16	230	100

$p < 0.1\%$ (In testing the spindle cell types have been grouped together and the fascicular excluded. In addition the groups of alive and died from other cause have been combined)

two years while half the patients with tumours of the mixed cell type do not die until five years after enucleation. The curve for the spindle cell types falls



1a



1b



2a



2b

Fig 1A

Photograph of the right fundus taken on 6th February 1969 Haemorrhages and exudates are visible above the optic disc

Fig 1B

Photograph of the right fundus taken on 23rd December 1969 A venous occlusion an arteriolar lesion (?) and neovascularization are seen situated above the haemorrhages shown in Fig A

Fig 2

Photograph of the right (A) and left (B) fundus taken on 6th February 1969 Phlebitic lesions of the main lower venous branches are visible Segmental sheathing of the vessel wall obscures the blood column. Small perivascular haemorrhages and exudates are seen

and did not show any other abnormality After the fluorescein had reached the arteriole which appeared to be almost completely occluded at ophthalmoscopy (Fig 1B) the newly formed vessels filled immediately (Fig 4) They dif

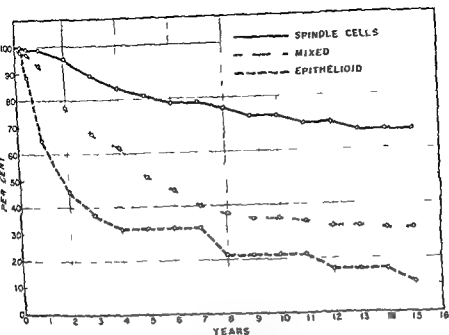


Fig 1

Actuarial survival curves for malignant melanomas of the choroid and ciliary body by cell type based on 230 cases

slowly at first whereas those for the mixed and epithelioid types fall more steeply. After about seven or eight years the three curves run approximately horizontally indicating that the chance of dying with metastases after this term of years is small for all patients regardless of the cell type of their tumour. The present new follow up shows however that dying with metastases still takes place within all groups of tumour.

Prognosis in relation to pigment content can be seen in Table 7 (Table 56) and the corresponding survival curves in Fig 2. The testing showed that the prognosis appears to be better for patients with tumours poor in pigment than for those heavily pigmented.

Where the reticulin content is concerned no significant difference in prognosis could be found between patients having had tumours rich in reticulin and those with a poor content. It must be stressed that some of the examined material was rather old which might have influenced the result of the reticulin staining.

Iris melanomas The ten cases of iris melanoma in seven males and three females of which one was a 1 year old girl showed unchanged results at the recent follow up. Three had died of whom only one with metastases present.

ferred in shape and calibre forming a fan like pattern and appeared to originate from this arteriole. After filling the newly formed vessels the dye was seen to pass rapidly through the blood retinal barrier and into the retina a large part of which became fluorescent (Figs 3 and 4). The leakage of dye originated from arterioles and capillaries and probably also from venules. The intensity of the fluorescence increased gradually and a few minutes after injection of the dye fine structural details of the fundus were obscured.

An extravascular fluorescent spot which fused with a small haemorrhage was seen in the lower part of left fundus. Other fluorescent spots which were not related to large vessels appeared in the early venous phase (Fig 5). These were probably due to leakage of dye from precapillaries or capillaries. Profuse leakage of dye from the oedematous optic disc was also shown (Fig 4).

From the beginning of the early venous phase until the end of the examination leakage of fluorescein occurred through the part of the vein wall showing segmental sheathing and a broad fluorescent band gradually formed around the vessels (Fig 5). There was no evidence either of occlusion of the lumina of veins or of circulatory congestion in this area. The intensity of the extravascular fluorescence increased the fluorescent band being still clearly visible nine minutes after injection of the dye. At that time the individual blood vessels did not contrast with the background the dye being evenly distributed in the tissues.

During the following ten weeks the patient was given corticosteroid therapy

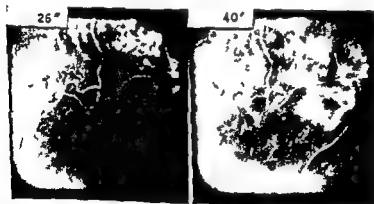


Fig 3

Fluorescein angiogram of right fundus taken on 23rd December 1969. Neovascularization and leakage of dye within the area of the retina shown in Fig 1B are visible. The digits indicate the interval in seconds between the injection of fluorescein and the taking of the pictures.

on a) sex and age b) the size of the tumour c) scleral invasion d) cell type e) pigment content and f) localization in the uvea (iris melanomas)

a) *Sex and age* Better prognosis for pre menopausal women has also been reported for cutaneous melanomas (5 17 20), and removal of the testes is reported to have improved the condition in a patient with metastases from a malignant choroidal melanoma (13)

Several cases are reported (6 11 18 21 23) where patients with malignant melanomas occurring during pregnancy have a particularly bad prognosis and chloasmata and hyperpigmentation in pregnant women are well known phenomena as also is a fair skin in eunuchs who do not readily become sunburnt These facts indicate some hormonal influence on the melanocytes Some writers however deny a causal correlation between pregnancy and tumour development (6) The exact mechanism of the hormonal influence especially the sex hormonal on melanin production is not known For survey and discussion of the problem reference is made to *Frenkel & Klein* (11)

b) *Size* The finding by *Flocks et al* (10) that a critical size of the melanoma with a view to the prognosis is about 1000 mm³ is important because it has enabled the clinician to observe the patient with good confidence over a longer period of time so as to become as certain as possible that he is dealing with a malignant neoplasm Many unnecessary enucleations can be avoided when this attitude towards neoplasms suspicious intra ocular processes is followed As previously reported (15) our series shows a better prognosis for tumours of less than 100 mm³ and if this area can be correlated to a volume of 1000 mm³ which I think is reasonable the Danish material is co incident with the American

The above mentioned writers (10) found small tumours usually to be pure spindle cell tumours and attribute the favourable prognosis to this cytologic characteristic (see below) An analysis of the present series in relation to this correlation showed no significant difference On the other hand an analysis of the material showed that the larger the tumour the greater the tendency to penetration inwards as well as outwards and as can be seen in Table 5 case with scleral invasion and extrascleral extension carry an unfavourable prognosis An analysis of these cases of invasion showed no significant overweight of anaplastic cell types

d) *Cell type* The prognosis of the individual case is dependent upon many single factors which have to be evaluated as a whole The cell type is probably the best single parameter As found in the previous follow up and in much other material tumours consisting of spindle cells have a much better prognosis than the anaplastic types Our material of the fascicular type is so small that it is not possible to compare the prognosis of cases of this cell type with the prognosis of those of the spindle B type *Zimmerman* (24 25) grouped these types together prognostically Our feeling has previously been that the fascicular type carried a less favourable prognosis than the spindle B cell type However no further

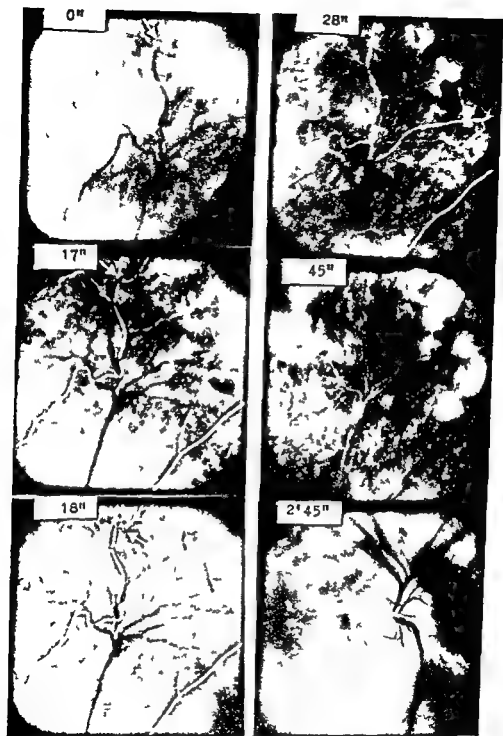


Fig 4

Fluorescein angiogram of the upper part of right fundus taken on 20th February 1960 i.e. two months later than those shown in Fig 3. Arrow points towards a venous occlusion and an affection of an arteriole (?). 18 shows newly formed vessels in the arterial phase. Profuse leakage of dye into the retina is visible (cp Fig 3). 2'45 shows the oedematous disc to be brilliantly fluorescent. The digits indicate the interval in minutes and seconds between the injection of fluorescein and the taking of the pictures.

deaths with metastases present have taken place since the last follow up in this little group of the present series so he may be correct in grouping them together

Zimmerman (25) still groups together tumours of the mixed and the necrotic cell types. In our experience necrotic tumours first of all originally belong to the most anaplastic type i.e. the epithelioid. In the present series no tumour was so necrotic that classification was impossible. In all cases of nearly total necrosis the remaining cells were epithelioid. In our opinion the necrotic group should be omitted from the classification since necrosis is not an adequate histopathological feature for classifying a tumour. Further in our opinion it is doubtful whether a classification having more than three groups is justified. Morphological classification of most malignant neoplasms ends in a tripartition i.e. a differentiated group, an anaplastic group and a group in between. Our experience (9) concerning the ultrastructure of malignant melanomas strengthens little by little our impression that this tripartition is also a more realistic grouping for malignant choroidal melanomas.

e) Pigment content. The present analysis again confirms the fact that highly pigmented tumours are the more malignant. This was also recently found by Marquardt (19). This writer expresses the same surprise as was our experience. It was to be expected that melanin production was a highly differentiated characteristic of the melanocyte so that the more pigmented the tumour the more differentiated the cells and the better the prognosis. First of all it must be pointed out that dedifferentiation may express a disturbance which affects only one or a few of the many cell functions and if this disturbance affects the melanin production it does not *a priori* mean a decreased production. Secondly in my experience much of the pigment seen in the highly pigmented (and malignant) melanomas is lying in melanophages indicating a rapid turn over so that the malignancy might be expressed in loss of a normal inhibition or control of the synthesis. According to Gordon (12) malignant melanomas may perhaps arise as a result of inhibition of the normal melanocyte development so that mature melanocytes will not be formed. On the contrary immature melanoblastic cells characterized by a strong melanin production will be the result.

f) Localization (iris melanomas). The present series showed a significant over weight of tumours localized temporally and posteriorly [Table 2]. Marquardt (19) found a better prognosis for melanomas with an origin at the equator. No difference in prognosis for tumours localized in different parts of the choroid could be found in the present series. All choroidal and ciliary body tumours were found to carry the same prognosis. The iris however harbours melanomas which differ clinically, histopathologically and prognostically from melanomas of the two other parts of the uvea. The average age of the present small series was 10 years lower than for the choroidal tumours. They were slow growing making the past history long and they were mainly symptomless. Only one in

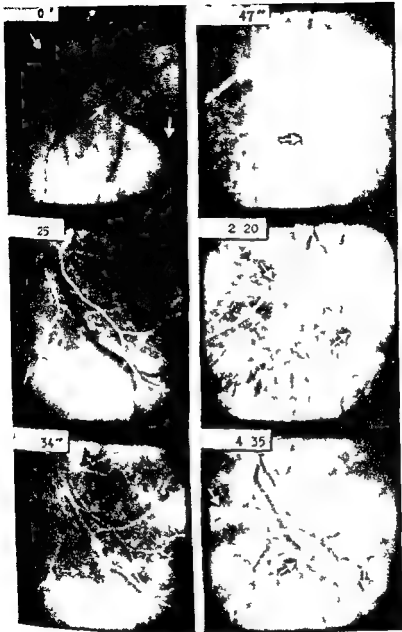


Fig. 5
 Fluorescein angiogram of left fundus taken on 3rd March 1969. The main lower branches of the retinal veins are visible. 0 shows periphlebitic lesions (arrows). 2 20 and 4 35 retention of dye in the inflammatory foci are shown. 34 and 47 show a fluorescent spot representing leakage of dye from precapillaries or capillaries (arrows). The dots indicate the interval in minutes and seconds between the injection of fluorescein and the taking of the pictures.

ten died with metastases within an observation period of 15 years. At the Ophthalmic Tumour Centre we have a very conservative attitude towards iris melanomas. During observation it is especially important to notice the size of the tumour, its relation to the chamber angle, the appearance of vessels in the iris or on the sclera, any darkening of the process or increase of pigment in the chamber angle.

If the process is progressing we advise conservative surgery mainly in the form of segmental resection of the iris and ciliary body or iridectomy if the tumour is located centrally near the pupillary margin. The long term results of this procedure cannot be determined on the basis of our material at present but large series (4-22) appear to justify this practice. The favourable prognosis of the present series was based on enucleation in all ten cases.

Conclusion and Summary

In Denmark from 1943 to 1952 a total of 305 malignant uveal melanomas was registered. Ten were localized in the iris. The average population was 4.1 millions. The clinical, histopathological and prognostical aspects of this series have previously been published (14).

The present recent follow up deals mainly with the prognosis on a 15 year observation period and with the therapeutic attitude of the Ophthalmic Tumour Centre towards special problems in the management of malignant uveal melanomas. At the date of follow up 72 per cent had died. The follow up percentage was 99. The frequency of orbital recurrence was 2.5 per cent and 0.3 per cent of the whole series had died with metastases present based on a 15 year observation period. On the basis of experience and the study of the ultrastructure of the tumour a classification of three groups, i.e. a differentiated, an anaplastic and a mixed group seems more realistic than the classical Callender classification.

The prognosis was estimated in relation to various clinical and histopathological characteristics. The prognosis was found to be significantly better for women under the age of 40, for small tumours of less than 100 mm, for cases without scleral invasion or extrascleral extension, for spindle cell tumours, for unpigmented or slightly pigmented tumours, and for iris melanomas. For the clinician a fundal process of small size and a peripheral location in the iris are particularly useful as both enable him without risk to observe the patient over a longer period of time making certain that the eye is not dealing with a malignant neoplasm. Growth of the process and its infiltration of the eye are still the only reliable clinical signs of a malignant neoplastic process. The prognosis will not deteriorate if the patient is observed until growth is established.

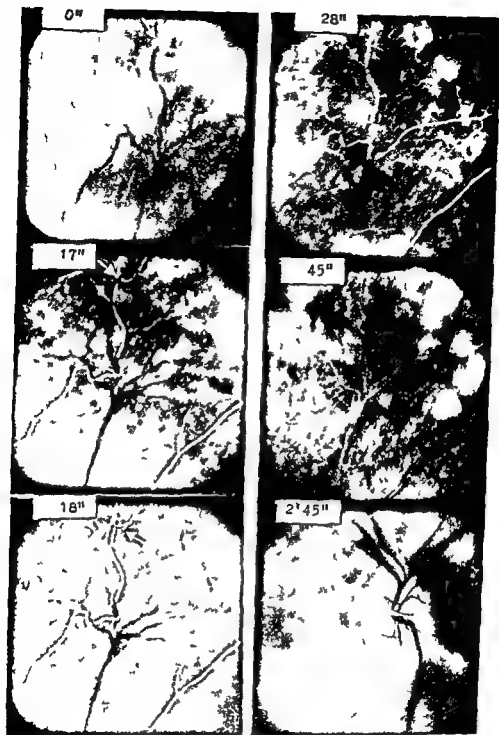


Fig 4

Fluorescein angiogram of the upper part of right fundus taken on 20th February 1970 i.e. two months later than those shown in Fig 3. Arrow points towards a venous occlusion and an affection of an arteriole (²). 18 shows newly formed vessels in the arterial phase. Profuse leakage of dye into the retina is visible (cp Fig 3). 2.45 shows the oedematous disc to be brilliantly fluorescent. The digits indicate the interval in minutes and seconds between the injection of fluorescein and the taking of the pictures.

This conservative attitude has been practised in the Ophthalmic Tumour Centre since its establishment in 1964 and it is our experience since the enucleated eyeballs are also histopathologically examined by the same team that the 22 per cent of mistaken diagnoses during the years 1943-1952 has decreased considerably probably to below 5 per cent (2)

Modern diagnostic methods such as ultrasonography and fluorescein angiography have of course also contributed to a better diagnosis

Our attitude towards blind and painful eyes especially eyes with intrasclerotic media, is radical Enucleation is advised since such eyes often harbour a malignant tumour Exenteration of the eyeball is contra indicated in these cases

Acknowledgement

The statistics were kindly checked by cand. stat. Knud West Andersen.

References

- 1 Allen J C & Jaeschke W H Recurrence of malignant melanoma in orbit after 28 years Arch Ophthal 16 19-81 1966
- 2 Andersen S R Intraocular tumour pathology and its relation to clinical ophthalmology Ophthalmologica (Basel) 160 18-41 1970
- 3 Andersen B & O'Neill J Malignant melanoma of the uvea Observations on growth and behaviour enucleation refused or delayed Arch Ophthal 58 337-347 1957
- 4 Ashton V Primary tumours of the iris Brit J Ophthal 48 650-663 1964
- 5 Brandt G Melanoma of the skin Thesis Munksgaard Copenhagen 1956 p 6
- 6 Borner R & Goder G Melanoblastom der Uvea und Schwangerschaft Klin Mbl Augenheilk 149 634-693 1966
- 7 Callender G R Malignant melanotic tumors of the eye A study of histologic types in 111 cases Trans Amer Acad Ophthal Otolaryng 36 131-142 1931
- 8 Murphy E B et al The diagnosis and management of intraocular melanomas A symposium Trans Amer Acad Ophthal Otolaryng 6 31-55 543
- 9 Egeberg J & Jensen O A Unpublished results
- 10 Flück M Gerende J H & Zimmerman L E The size and shape of malignant melanomas of the choroid and ciliary body in relation to prognosis and histologic characteristics Trans Amer Acad Ophthal Otolaryng 59 40-753 1955
- 11 Frenkel M & Klein H Z Malignant melanoma of the choroid in pregnancy Amer J Ophthal 62 910-913 1966
- 12 Gordon M The melanoma cell as an incompletely differentiated pigment cell In Gordon M (Ed) Pigment Cell Biology Academic Press Inc New York 1959 p 233

wall of the veins to be thickened with multiple foci of epithelioid cells and lymphocytes which were arranged in the form of grapes (traubenformig ange lagert). *Levitt* (1941) observed the association of retinal periphlebitis and arteritis in sarcoidosis and reported that characteristic features of these cases were mantling of the vessels with sarcoid tissue causing occlusion of the lumina of many vessels or complete replacement of the vessel wall by epithelioid cells. According to *Michaels et al* (1960) a similar type of arteritis of the pulmonary blood vessels may be found in sarcoidosis.

The case presented in this paper illustrates the typical periphlebitis retinae and the extremely rare arteritis which may be associated with sarcoidosis. The arteriolar occlusion appeared to be almost complete as seen in the ophthalmoscope. Fluorescein angiography however did not reveal a complete occlusion but showed newly formed vessels originating from this place. Fluorescein studies of retinal arteriolar occlusions in hypertension and arterio sclerosis have shown that recanalization of occluded vessels often occurs. In the case presented the formation of new vessels suggests that a pathological process had involved arteriolar tissue. This process may have been a primary arteriolar sarcoid or it may have been due to the adjacent phlebitis.

These types of vascular lesion are highly permeable to fluorescein. As most of the dye is bound with serum albumin (*Hodge & Dollery* 1964) plasma proteins and in severe cases probably also blood corpuscles pass through the vessel wall. In contrast to normal tissue inflammatory tissue around the vessel wall retains fluorescein. The retention of fluorescein in inflammatory tissue has been observed in conditions such as choroiditis. Thus the vascular changes revealed by fluorescence angiography in the case discussed correspond to those said to be present in sarcoid vasculitis.

As there was no angiographic evidence of choroidal involvement in our case the fundus lesions appear to have been limited to the retina. *Shikano & Shimizu* (1968) encountered 3 cases of fundal sarcoidosis in which the retinal circulatory system alone was involved whilst Bruch's membrane and the choroid did not show any abnormality.

The clinical and angiographic picture of the vasculitis retinae in the case here presented resembled in many respects those associated with idiopathic perivasculitis (Eales' disease) except for the co-existent anterior uveitis. The high incidence of the association of uveitis and vasculitis retinae was emphasized by *Cross* (1963). The etiology of the retinal lesions may be easily overlooked if the sarcoid iridocyclitis is deficient in characteristic symptoms. *Jutte & Lemke* (1966) observed that idiopathic periphlebitic lesions (Eales' disease) were highly permeable to fluorescein but considered the blood retinal barrier to be unaffected by the vascular changes which occur in uveitis. The observations made in the case presented did not support these findings.

- 13 *Herbst W P* Malignant melanoma of the choroid with extensive metastasis treated by removing secreting tissue of the testicles *J Amer med Ass* 122 597 1945
- 14 *Jensen O A* Malignant melanomas of the uvea in Denmark 1943-1952 Thesis Copenhagen 1965 p 53-55
- 15 *Jensen O A* Malignant melanomas of the choroid in Denmark Extract from the Danish Medical 1943-1952 *Mod Probl Ophthal (Basel)* 7 56-60 1968
- 16 *Jensen O A & Andersen S R* Late complications of biopsy in intraocular tumors *Acta ophthal (Kbh)* 37 568-575 1959
- 17 *Lancet* (Leading article) Malignant melanoma *Lancet II/61* 585-586 1961
- 18 *Lederman M* Radiotherapy of malignant melanomata of the eye *Brit. J Radiol* 34 21-42 1961
- 19 *Marquardt R* Untersuchungen zur Prognose der malignen Melanome der Gefasshaut des Auges *klin Mbl Augenheilk* 150 51-56 1967
- 20 *Olsen G* Maligne melanomer i huden. *Ugeskr Læger* 123 1235-1244 1961
- 21 *Reese A B* Tumors of the eye 2 ed Hoeber Medical Division New York Evanston and London 1963 ■ 218
- 22 *Rones B & Zimmerman L E* The prognosis of primary tumors of the iris treated by iridectomy *Arch Ophthal* 60 193-205 1958
- 23 *Timm G* Personal communication 1965
- 24 *Zimmerman L E* The registry of ophthalmic pathology Past present and future. *Trans Amer Acad Ophthal Otolaryng* 67 51-113 1961
- 25 *Zimmerman L E* Changing concepts concerning the malignancy of ocular tumors *Arch Ophthal* 78 166-173 1961

For further references see the bibliography of 14

Fluorescein angiography carried out after the completion of this treatment showed that the phlebitic lesions had disappeared and the appearance of the veins were normal (Fig 6). Only a few discrete haemorrhages, the venous occlusions and the newly formed vessels were visible in the right fundus.

Discussion

Mylus & Schurmann (1929) were the first to describe the histological appearance of phlebitic retinal lesions associated with sarcoidosis. They found the

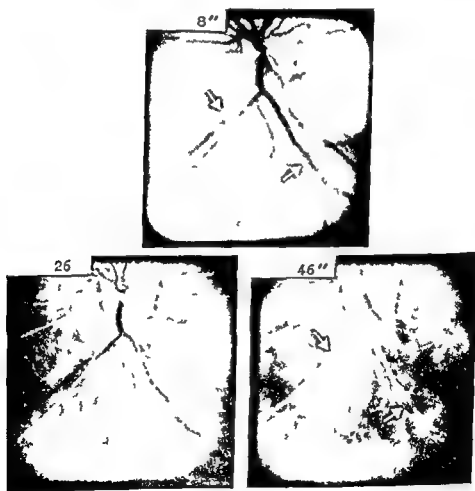


Fig 6

Fluorescein angiogram of the lower part of the left fundus taken on 19th May 1969 and about ten weeks after those shown in Fig 5. There is no evidence of phlebitic lesions (arrows). The digits indicate the interval in minutes and seconds between the injection of fluorescein and the taking of the pictures.

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FLUORESCEIN STUDIES OF RETINAL VASCULITIS IN SARCOIDOSIS

Report of a Case

BY

PEEP ALQVERE

Involvement of the ocular fundus in sarcoidosis probably occurs more frequently than is generally recognized. Geeraets *et al* (1962) observed fundus involvement in 40 out of 133 cases of sarcoidosis which they had studied clinically.

The most common fundus manifestations of sarcoidosis include perivascular infiltrates resembling candle drippings (Franceschetti & Babel 1949), retinochoroiditis, nodules, granulomas and papillitis. For a review of these conditions the reader is referred to Gould & Kaufman's paper (1961) and Duke Elder's System of Ophthalmology (1966).

von Bahr (1938) was the first to report a case of uveoparotitis associated with sheathing of retinal veins. His report was followed by numerous papers on sarcoid involvement of the retinal vessels (Walsh 1939, Meyer 1939, Lindau & Löwgren 1940, Leitch 1941, Wagner 1941, Goldberg & Newell 1944, Tiong 1949, Cross 1955, Jütte & Lemke 1965, Fontan *et al* 1966). These cases usually show perivascular mantling with inflammatory tissue and perivascular distribution of patches of exudate and oedema.

Occlusion of the lumen of the vessels may occur and may cause superficial

- Meyer Fr W Augentuberkulose und Lymphogranulomatosis benigna. (Boecksches Sarkoid multiples benignes Miliarlupoid) Klin Monatsbl Augenh 1939 102 16
- Michaels L Brown A J & Cory Wright M Arterial changes in pulmonary sarcoidosis A M A Arch Pathol 1960 69 141
- Mylus A & Schurmann P Universelle sklerosierende tuberkulose grosszellige Hyperplasie eine besondere Form atypischer Tuberkulose Beitr Klin Tuberk 1929 13 163
- Novotny H R & Alvis D L A method of photographing fluorescence in circulating blood in the human retina Circulation 1961 24 52
- Quock C P & Donahoe R F Flame shaped retinal hemorrhages in sarcoidosis J A M A 1961 187 939
- Rosen E S Fluorescence photography of the eye Butterworth & Co Ltd London 1969
- Shikano S & Shimizu A Atlas of fluorescence fundus angiography Igaku Shoin Ltd Tokyo 1968
- Tiong Y A Een geval van Boecks sarcoid van het oog Nederl tijdschr geneesk 1949 93 1643
- Wagner H Augenveränderungen bei Boeckscher Krankheit Klin Monatsbl Augenh 1941 106 29
- Walsh F B Ocular importance of sarcoid Its relation to uveoparotid fever A M A Arch Ophth 1939 21 471
- Wessing A Fluoreszenzangiographie der Retina G Thieme Verlag Stuttgart 1968

Thygeson (1956) found 10 per cent to recover spontaneously while *Larsson* (1964) saw 24.5 per cent to be cured after placebo treatment alone. *Burns* found placebo and IDU to be equally effective in the treatment of chronic keratitis or relapses. *Davidson* obtained healing of dendritic keratitis in half of his patients within 14 days of instillation of 1 per cent gamma globulin which he himself regarded as a placebo.

The immediate success of a treatment (fading of the dendritic pattern and shadowy transformation on IDU treatment and decreasing ciliary congestion on steroid treatment) need not indicate a favourable response at the long view.

To study the effect of the treatment given I have followed up just over 100 patients to compare the therapy with two of the parameters on which an evaluation of the therapeutic effect on the long view may be based namely the recurrence rate and the visual acuity at the time of the follow up.

Present Investigations

The investigation comprised all the patients referred within a seven year period (1958-1964) to the Department of Ophthalmology *Kommunehospitalet* with dendritic keratitis i.e. a corneal affection presenting a typical dendritic pattern.

This characteristic disease was described as early as 1884 by the first professor of ophthalmologiae in Denmark *Edmund Hansen Crut* (keratite ramifiée).

No virus cultivation was performed to verify the herpetic affection the morphological picture being generally regarded as sufficiently specific to justify a diagnosis of herpetic keratitis.

Incidence

Within the seven year period 157 patients were seen who had had one or more attacks of dendritic keratitis i.e. 22.4 patients annually.

Several of these patients experienced renewed attacks within the seven year period. Thus a total of 287 attacks were recorded of which some repeated i.e. 41 attacks annually.

During the same period 6062 patients were admitted to the Ophthalmic Unit while 50270 were treated as out patients. Among these a total of 952 had keratitis of some kind or other. The recorded cases of dendritic keratitis constituted 1/96 of the total number with ophthalmic diseases.

during the first few days of the disease at the subsequent stages IDU hardly does any good (*Jepson Davidson*)

IDU is cytotoxic This explains perhaps the poor effect at the more advanced stages when the virus may be gone and when the epithelial healing does not run a satisfactory course owing to the continued IDU treatment (*Burns*)

Treatment with *steroids* has been extensively discussed and dearly bought experience has been gained from such treatment It is universally agreed that steroid treatment may reduce the resistance of the tissue to bacteria and fungi Steroids may provoke herpetic eruptions Steroids should not be used at the acute stage of herpes

During the subsequent – metaherpetic – phase steroid therapy has been recommended under IDU cover from the view that the metaherpetic phase is due to allergic reaction to the virus in the epithelium Steroid treatment reduces the oedema of the corneal parenchyma thus counteracting cicatrization and visual impairment

Kaufman (1964) has recommended steroid in cases of geographic ulcer which may follow dendritic keratitis According to Kaufman this ulcer contains no virus actually corresponding to a recurrent erosion Kaufman does not use IDU simultaneously with steroid against geographic ulcer in order not to counteract the tendency to healing

The results of recent investigations suggest however that the herpes virus has not been eliminated at these late stages The virus has been demonstrated in the lacrimal gland (*Kaufman* 1968) the conjunctiva (*Brown Jones Kaufman*) and in the corneal parenchyma (*Dawson et al*) at the clinically inactive stage

Thygeson (1967) warns definitely against steroid therapy owing to his experience regarding a new disease described by him This is termed chronic herpetic kerato uveitis and is a sequela of steroid treated herpetic keratitis The disease persists for years and flares up each time discontinuation of the steroid treatment is attempted

The disease is possibly due to the steroids interfering with the immune mechanism in such a way that the local virus infection of the avascular corneal tissue cannot be brought to a conclusion

A third possibility of treating herpetic keratitis is that of applying *tincture of iodine alcohol phenol or lunar caustic* locally on the process

This treatment is painful but often efficient (*Gundersen*)

The objection may be raised to this therapy that herpes may be activated by a trauma (*Nataf et al*) Such cauterization is in fact a trauma which may aggravate instead of eliminating the affection

In assessing the various therapeutic possibilities we must not forget that this virus provoked disease tends to spontaneous cure (*Jepson* and others)

The spontaneous course has rarely been studied because the doctor is disinclined to forbear a treatment which may improve an impaired vision

Summary

A case of sarcoidosis associated with pulmonary changes uveoparotitis bilateral anterior uveitis and inflammatory reaction of the vitreous is reported in which the patient developed bilateral vasculitis retinae There was ophthalmoscopic evidence of venous occlusion neovascularization oedema of the optic disc and multiple foci of periphlebitis

Fluorescein angiography revealed profuse leakage of dye from newly formed vessels and the optic disc and retention of dye by perivascular inflammatory infiltrates

The vascular lesions in the case reported resembled those associated with Eales disease

References

- von Bahr G A case of uveo parotitis with perivasculitis and other rare symptoms
Acta ophth 1938 16 101
- Cross A G Ocular sarcoidosis *Tr Ophth Soc U Kingdom* 1955 75 181
- Cross A G Vasculitis retinae *Tr Ophth Soc U Kingdom* 1963 83 133
- Dow D S Ocular sarcoidosis Report of a case characterized by vitreous and retinal hemorrhages extensive periphlebitis anterior uveitis and secondary glaucoma and with multiple system involvement *Am J Ophth* 1965 59 93
- Duke Elder S Diseases of the uveal tract *System of Ophthalmology Vol IX* H Kimpton London 1966 p 517
- Fontan P Pernod J Cug G & Guillermin R Sarcoides de la retine *Bull Soc ophth France* 1966 66 37
- Franceschetti A & Babel J La chorio retinite en taches de bougie manifestation de la maladie de Besnier Boeck *Ophthalmologica* 1949 118 101
- Geeraets W J McNee K W Macey E F & Cherry D Retinopathy in sarcoidosis
Acta ophth 1962 40 492
- Goldberg S & Newell F W Sarcoidosis with retinal involvement Report of two cases *A M A Arch Ophth* 1944 32 93
- Gould H & Kaufman H E Sarcoid of the fundus *A M A Arch Ophth* 1961 65 453
- Hodge J V & Dollery C T Retinal soft exudates A clinical study by colour and fluorescence photography *Quart J Med* 1964 33 117
- Jutte A & Lemke L Fundusveränderungen bei Morbus Boeck *Ophthalmologica* 1965 149 3
- Jutte A & Lemke L Kapillardefekte im Netzhautkreislauf bei Periphlebitis retinae
Klin Monatsbl Augenh 1966 149 334
- Levitt J M Boeck's sarcoid with ocular localization Survey of the literature and report of a case *A M A Arch Ophth* 1941 26 358
- Lindau A & Louegren A Benign lymphogranuloma (Schaumann's disease) and the eye *Acta med scandinav* 1940 105 242

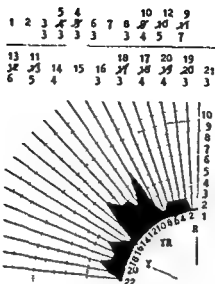


Fig 1

Specimen of Farnsworth Munsell 100 Hue score and profile

of 16 and 35 years (*Lakowski* 1958) After 35 years there is a rapid deterioration in the ability for fine colour discrimination which affects mainly yellow blue or violet blue green discrimination Red green discrimination remains fairly stable and is least affected by age *Verriest* (1963) demonstrated that in normal healthy subjects the error score for the Farnsworth Munsell Hundred Hue test increased in a positive manner with age from the age of 35 onwards At the age of 60 years he quotes a mean error score of 95 with an upper limit of 152 for men

Untreated Tobacco Amblyopia

A group of 65 patients of mean age 67 years was composed of 64 males and one female of whom 57 smoked pipe tobacco only 3 cigarettes only and 5 both The mean tobacco consumption of the group was 3.04 ± 1.44 ozs per week They were diagnosed as suffering from tobacco amblyopia after the criteria of *Heaton et al* (1958) The mean error score for the right eye of all patients for the Farnsworth Munsell Hundred Hue test was 732 ± 236 In an earlier communication (*Chisholm* 1969) it was suggested that in the case of error scores above 600 a mean of several test results be taken and below 600 a single test result would be sufficiently reliable Where possible this premise was adhered to A typical 100 Hue profile in untreated tobacco amblyopia shows depressed dis

than those of the Mackay Marg tonometer (MMT). However, in comparative studies performed just the opposite was true. The MMT - pressure values (P_{MMT}) were as a rule higher than those of the applanation tonometer (P_{AT}) (Moses *et al* 1962 Hilton *et al* 1966 Tierney *et al* 1966 Suda *et al* 1967 Follmann *et al* 1969).

In a more recent study (Stepanik 1970) the difference $P_{MMT} - P_{AT}$ proved to be dependent on the level of the intraocular pressure and on the rigidity coefficient of the measured eye and the increase of the intraocular pressure P_0 to P_{MMT} to be equal to a pressure increase produced by a corneal applanation of 4.9 mm in diameter.

To elucidate this statement deduced from clinical measurements by calculation, the following experimental study was performed. Over a window of a transparent pressure chamber connected to a watermanometer the cornea plus the anterior segment of the sclera of 4 enucleated human eyes was mounted on the slitlamp (Haag Streit Model 900) in such a manner that the cornea could be observed from the inside of the chamber whereas the MMT probe was brought in touch with the cornea from outside (Fig. 1). The size of the applanated corneal area was distinctly visible through the cornea in blue light outlined by a fluorescein ring as well as in the optical section. The footplate of the MMT's probe used in this study (Model 200 S/N 4550 Berkeley Tonometer Company California) has a diameter of 4.8 mm, the sensitive area in its center a diameter of 1.6 mm.

In this experiment set up it was easy to start the corneal applanation exactly at the center of the probe, to dissect the whole recording in sections and record them step by step in correlation to the observed sizes of corneal applanations.



Fig. 1

(Stepanik) Experimental set up. Transparent pressure chamber and the probe of the Mackay Marg tonometer mounted at the slitlamp of Haag Streit (Model 900).

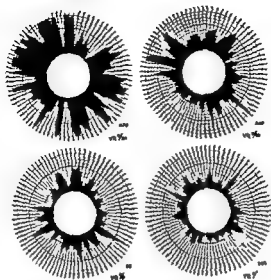


Fig 3

Alteration of Farnsworth Munsell 100 Hue profile with time on treatment with hydroxocobalamin. Raw scores and visual acuity are shown in untreated state and after 3 and 6 months therapy

We found that when the Farnsworth Munsell Hundred Hue error score was plotted against time on treatment a curve was produced which fitted the exponential equation $Y = A e^{-kt} + C$. When such an equation was converted to logarithms a straight line was produced whose slope was given by the value for k ($\log_e (Y-C) = \log_e A - kt$). Thus the value for k is an index of the rate of improvement of the patient's colour vision. The value for C is the value at which the exponential curve would become horizontal. It is an individual characteristic dependent on patient age and on the presence or absence of any ocular or systemic disease thought to cause an upset in colour discrimination. A computer was used to find the value for C which gave the best fit to individual patient data.

To illustrate this the following case may be considered. A 68 year old male who smoked 2.5 ozs pipe tobacco per week developed classical tobacco amblyopia. On treatment with hydroxocobalamin he improved. Fig 4 shows the Farnsworth Munsell Hundred Hue error score for his right eye plotted against time. With a C value of 20 the result of conversion to logarithms is indicated by Fig 5.

It is well recognised that patients with tobacco amblyopia show a high incidence of complicating systemic disease particularly of those diseases associated

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THE MACKAY - MARG TONOMETER

Correlation of the tonogram to the corneal applanations
induced by the tonometer

BY

JOSEPH STEPANIK

To eliminate extraneous factors such as rigidity in the corneal tissue to resist deformation and the surface tension of the tears Mackay & Marg (1959) devised a new electronic tonometer based on the following principle. The plane tip of a small hand held probe carries a pressure sensitive area in its center. Current that measures the force on this area is recorded as a function of time on a strip record.

Due to Mackay *et al* (1960) the recording reaches the first crest when the flattened cornea is in touch only with the sensitive area. The amplitude of this crest indicates the intraocular pressure plus the bending forces of the cornea and thus is the reading that is obtained by the classic applanation tonometers such as that of Goldmann. By further increase of the corneal applanation the plate surrounding the sensitive area sustains the bending forces and the sensitive region carries only the intraocular pressure. The recorded curve drops therefore to a trough the amplitude of which is a measure of the intraocular pressure.

Considering this interpretation of the recording it was to be expected that the readings of Goldmann's applanation tonometer (AT) should range higher

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In 51 patients a definite estimation could be made of the interval in months between the onset of symptoms and seeking medical advice. When this was compared with the Farnsworth Munsell Hundred Hue error score a positive relationship was found which was just significant ($r = +0.242$ $n = 49$ $0.1 > p > 0.05$). Thus poor colour discrimination tended to be associated with poor visual acuity, increased age and a long history of visual symptoms. It was found that patients over the age of 65 years sought medical advice within six months of the onset of symptoms as readily as those patients aged 65 years or younger ($x = 0.11$ $n = 55$ $p = 0.95$). Thus age and tobacco amblyopia play separate roles in the production of the acquired dyschromatopsia.

In recent years there has been increasing awareness of the part played by avitaminosis B12 in the aetiology of tobacco amblyopia (Carroll 1956; Heaton *et al.* 1958; Foulds *et al.* 1969 *a* and *b*). The serum vitamin B12 of these patients was assayed by the *Euglena gracilis* method after Ross (1952) and a range of concentrations from 15 pg/ml – 512 pg/ml with a mean at 196 pg/ml was obtained. There was no significant relationship between the serum vitamin B12 concentration and the Farnsworth Munsell Hundred Hue error score in our group of cases ($r = +0.161$ $n = 58$ $p > 0.1$).

Treated Tobacco Amblyopia

Apart from 5 all the patients were given parenteral vitamin B12 therapy. Initially they were given either cyanocobalamin or hydroxocobalamin. By observing the improvement in colour vision indicated by a falling 100 Hue error score it was clear that the hydroxocobalamin form of vitamin B12 was superior to the cyanocobalamin form in its therapeutic effect (Chisholm *et al.* 1967). All patients' therapy was subsequently altered to hydroxocobalamin at a dose of 1000 μ g daily for the first 14 days and then 1000 μ g thrice weekly. Adjustments were made dependent on the response. Patients were advised that it was not necessary to alter their smoking habit.

The improvement in colour discrimination may be observed by studying the change in the Farnsworth Munsell Hundred Hue profile or alteration in the numerical error score.

A 50 years old male developed classical tobacco amblyopia when smoking 1½ ozs pipe tobacco per week. He was treated with hydroxocobalamin and allowed to continue smoking. Fig. 3 shows his Hundred Hue profile initially and at 1, 3 and 6 months after the commencement of treatment. There has been a noticeable shrinkage in the areas of error, a reduction in the error score and a rise in visual acuity.

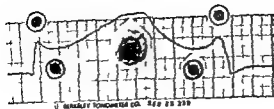


Fig 3

(Stepanik) The regular recording of the Mackay Marg tonometer and the corneal applantations correlated to its crests and troughs

Summary

In the Mackay Marg tonometer using a transparent pressure chamber on the slitlamp the size of the corneal applantations induced by the tonometer at the turning points of the tonogram were observed on 4 enucleated eyes. In this study the amplitude of the trough in the ascending part of the tonogram generally accepted as the reading of the intraocular pressure coincided with an applantation of the cornea by the whole footplate area of 4.8 mm in diameter.

Acknowledgement

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References

- Filman P & Karpatis A Appraisal of the Mackay Marg electronic tonometer in adults *Am J Ophthalmol* 179: 85 (1969)
- Hilton G F & Schaffer R V Electronic applantation tonometry *Amer J Ophthalmol* 69: 833 (1966)
- Mackay R S & Marg E Fast automatic electronic tonometers based on exact theory *Acta ophthalmol (Kbh)* 37: 495 (1959)
- Mackay R S, Marg E & Orchels R Automatic tonometer with exact theory Various biological applications *Science* 131: 1663 (1960)
- Moss R A, Marg E & Orchels R Evaluation of the basic validity and clinical usefulness of the Mackay Marg tonometer *Invest Ophthalmol* 1: 78 (1962)

with deficiency or increased requirement for vitamin B12. In our present group the following diseases were found

Addisonian Pernicious Anaemia	16.9%
Prc pernicious anaemia (evidence of pernicious anaemia without anaemia)	16.9%
Diabetes	9.3%
Hepatic disease	3.1%
Other conditions	6.1%
No systemic disease	47.7%

From the data the following groups of patients were available for comparing rates of improvement in colour vision i.e. values of k

Group	Mean value for k
(a) Tobacco amblyopia with no associated disease treated by abstinence from tobacco	0.302
(b) Tobacco amblyopia with no associated disease treated by hydroxocobalamin	0.294
(c) Tobacco amblyopia associated with diabetes treated by hydroxocobalamin	0.528
(d) Tobacco amblyopia associated with Addisonian pernicious anaemia treated by hydroxocobalamin	0.195
(e) Tobacco amblyopia associated with Prc pernicious anaemia treated by hydroxocobalamin	0.341

When the mean slopes for these groups of patients were compared (Fig. 6) it was found that the rate of recovery in tobacco amblyopia with no associated disease was as rapid if the patient was treated by abstinence from tobacco as that when treatment with hydroxocobalamin was given and the patient continued to smoke* ($t = 0.38$ $p = > 0.1$). The rate of recovery in tobacco am

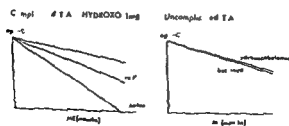


Fig. 6
Mean rates of improvement in colour discrimination

(Fig 2) When the fluorescein ring was still within the sensitive area of the probe (a) the record dropped slightly down below the zero line indicating obviously the capillary force of the contact fluid attracting the sensitive area towards the cornea. Then the pressure chamber was very slowly moved towards the MMT probe applanating progressively the cornea until the climbing pointer of the tonometer recorder just turned to go down (b). The border of the applanated corneal area was at the inner third of the footplate zone. Step c indicates the amplitude of the next turning point of the recorder from going down to going up. On that point the cornea was in touch with the whole footplate area the fluorescein ring framing the outer margin of the probe. Step d indicates the period of additional indentation of the cornea surrounding the footplate.

Pulling now the slitlamp gently backwards step e indicates the amplitude of the recording at the turning point from down to up corresponding to a corneal appplanation by the total footplate. f indicates the turning point from up to down at a corneal flattening with borders within the inner zone of the footplate and g again capillary traction of the fluid on the sensitive area free of cover when the fluid ring came in touch with the latter.

Thus in the ascending as well as in the descending part of the MMT recording (Fig 3) the crest corresponds to an appplanation of the cornea by the sensitive area plus the inner third the trough to a corneal appplanation by the sensitive area plus the whole footplate zone.

These experimental data prove therefore in splendid conformity with the results of the foregoing clinical study that the Mackay Marg tonometer does indicate the intraocular pressure at a corneal appplanation close or equal to 5 mm in diameter.

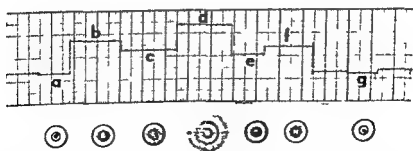


Fig 2

(Stepanik) Step by step registration of the turning points of the Mackay Marg tonometer's recording and the correlated contact areas of the footplate to the cornea as observed by the slitlamp

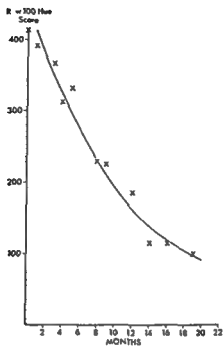


Fig 4

Raw 100 Hue error score plotted against time on treatment

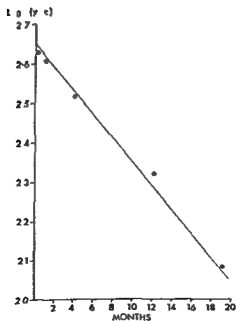


Fig 5

Data of Figure 4 converted to logarithms C value of 20 ($r = 0.99$)



Fig 3

(Stepanik) The regular recording of the Mackay Marg tonometer and the corneal applanations correlated to its crests and troughs

Summary

In the Mackay Marg tonometer using a transparent pressure chamber on the slitlamp the size of the corneal applanations induced by the tonometer at the turning points of the tonogram were observed on 4 enucleated eyes. In this study the amplitude of the trough in the ascending part of the tonogram generally accepted as the reading of the intraocular pressure coincided with an applanation of the cornea by the whole footplate area of 4.8 mm in diameter.

Acknowledgement

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References

- Follman P & Harpal A Appraisal of the Mackay Marg electronic tonometer in adults. *Acta Ophthalmol Scand* 1:8 83 (1969)
- Hilton G F & Schaffer R V Electronic applanation tonometry. *Amer J Ophthalmol* 61: 838 (1966)
- Mackay R S & Marg F Fast automatic electronic tonometers based on exact theory. *Acta ophthalmologica* 7: 495 (1959)
- Mackay R S, Marg E & Oechsli R Automatic tonometer with exact theory. Various biological applications. *Science* 131: 1663 (1960)
- Moses R A, Marg E & Oechsli R Evaluation of the basic validity and clinical usefulness of the Mackay Marg tonometer. *Invest Ophthalmol* 1: 78 (1962)

of the right eye in a patient suffering from classical tobacco amblyopia treated with hydroxocobalamin. It is apparent that the visual acuity has returned to normal levels before the ability for colour discrimination. It seems probable that the improvement in colour sense is not wholly dependent on visual acuity.

Discussion

Defective colour vision acquired by patients born with a potentially normal colour vision system develops through various stages the earliest of which is an abnormal trichromatic stage. Pseudo isochromatic plates are of little value in detecting this relatively early stage which however can be picked up by the Farnsworth Munsell Hundred Hue test.

Disease processes affecting the neuro sensory or conductive layers of the retina will if severe enough lead to blindness. Less severe disease will degrade visual function in a variety of ways including the development of an acquired dyschromatopsia. Thus lesions of the neuro sensory retina by and large result in a loss of colour discrimination in the yellow blue or violet blue green and lesions of the conductive layers in the red green areas of the spectrum respectively (Koellner 1912, Cox 1960, Verriest 1963).

Pigment matching tests of which the Farnsworth Munsell Hundred Hue test is a refined and useful example, test the subject's ability to discriminate between colours which differ only by a small amount when viewed under a constant illumination. This test enables a qualitative as well as a quantitative estimation of the colour defect to be carried out (Crone 1961). One of the great merits of the Farnsworth Munsell Hundred Hue test is that elements suitable for detecting colour confusion can also be used for detecting the variations in colour discrimination existing among trichromatic observers. To be able to measure these variations the tasks presented for discrimination must involve small colour differences such as are found in the Farnsworth Munsell Hundred Hue test. The differences between successive caps is of the order 2.5 NBS units. The task here may be considered analogous to visual acuity testing. Subjects with acute colour discrimination will arrange the colour series in each box within the two end limits correctly, those with lesser discrimination will accumulate error scores which are a measure of the degree of displacement from the ideal arrangement (Lokowski 1968).

Caleowiki (1883) was first to draw attention to the subjective colour defect of tobacco amblyopia and Groenouw (1892) pointed out that this acquired dyschromatopsia differed from that of the congenital dichromat. Cox (1960), François & Verriest (1961), Saraux et al (1966), Bounie & Coscas (1966) all record profiles showing defective red green discrimination in Tobacco Amblyo-

- Stepanik J* Das Mackay Marg Tonometer I klinische Studien *A v Graefes Arch klin exp Ophthal* 180 104 (1940)
- Suda K Tojohuku H & Muto K* Comparisons between Mackay Marg pressure readings and Goldmann or Schiotz pressure readings *Japan J clin Ophthal* 21 209 (1967)
- Turney J P & Rubin M L* A clinical evaluation of the electronic applanation tonometer *Amer J Ophthal* 62 263 (1966)

blyopia associated with diabetes was more rapid than when tobacco amblyopia was associated with Addisonian pernicious anaemia* ($t = 2.45$ $p = 0.05$)

The outlook for good visual recovery was as good in tobacco amblyopia unassociated with systemic disease and treated by hydroxocobalamin as in tobacco amblyopia associated with diabetes and treated by hydroxocobalamin* ($t = 0.80$ $p = > 0.1$) The rate of recovery of colour discrimination was slower in those patients whose tobacco amblyopia was associated with evidence of pernicious anaemia than in any other group The mean period of treatment with hydroxocobalamin at full dosage of these patients was 20.4 months before a good standard of vision was achieved This is prolonged when compared with the mean of 6.82 months of those patients with tobacco amblyopia unassociated with systemic disease Of the 63 patients 6 were experiencing a recurrence of the disease and of these 3 had pernicious anaemia It is possible that these patients had never fully recovered from their previous bout of tobacco amblyopia which had been treated by abstinence from tobacco In each of these cases the recurrence had occurred after an interval of not less than 7 years

(* Fractional weighted t test)

We have found tests of Hue discrimination a more sensitive indicator of visual improvement than visual acuity and confirm Riddell's (1936) findings that the return of colour vision takes longer than the central visual acuity Fig 1 illustrates the rate of visual improvement and recovery of colour discrimination

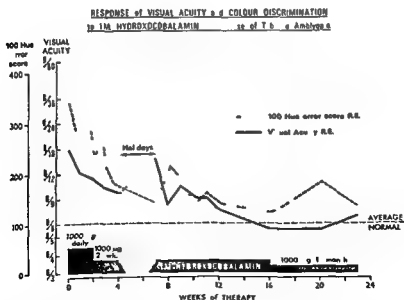


Fig 7

Plot of visual acuity and Farnsworth Munsell 100 Hue with time on treatment illustrating the disproportion between rate of visual and colour discrimination improvement

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COLOUR VISION IN TOBACCO AMBLYOPIA

BY

J A CHISHOLM J BRONTE STEWART and
E O AWDUCHE

One of the diagnostic criteria of tobacco amblyopia is the finding in the centro caecal area of the field of vision of depressed sensitivity to red and green stimuli. This is accompanied by a subjective disturbance of colour discrimination. Of the tests available for studying this acquired colour defect, we have found the Farnsworth Munsell Hundred Hue test although time consuming most useful. This paper reports the results of an investigation by means of this test into the colour vision of patients suffering from treated and untreated tobacco amblyopia.

The Farnsworth Munsell Hundred Hue test (Farnsworth 1943) originally designed for the binocular screening of youthful subjects for congenital colour blindness consists of a graded series of 85 coloured caps arranged in 4 boxes. The patient is required to arrange the coloured caps into a regular colour sequence between fixed end caps. He is presented with the coloured caps arranged in a standard random fashion. In the tests carried out by us no time limit was set for the completion of each box as many of the patients in addition to having defective visual acuity had difficulty in manipulating the caps. The tests were carried out on each eye separately using artificial illumination provided by the Hubble Verwide Cabinet which satisfies British Standard 900 part I (1967). The patient's arrangement of the caps is recorded and from this his error score can be calculated and expressed numerically or graphically (Fig 1).

Colours are perceived and discriminated most accurately between the ages

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cine in relation to Mathematics and Computing gave helpful advice on the statistical evaluation of the results Financial aid for this investigation was provided by the Mc cline in relation to Mathematics and Computing gave helpful advice on the statistical dical Research Council and Glaxo Ltd

References

- 1 Bouniq C & Costas G (1966) Etude Statistique et Analytique de 164 cas de Nev rite Optique Alcoololo tabagge Ann Doculist 199 9.5
- 2 British Standard 950 part 1 (1967) Artificial Daylight for the Assessment of Colour British Standards Institution London
- 3 Carro F D (1956) Toxic Amblyopia Trans Amer Acad Ophth 60 74
- 4 Chisholm I A (1969) An Evaluation of the Farnsworth Munsell Hundred Hue test as a Clinical Trial in the Investigation and Management of Ocular Neurologi cal Deficit Trans Ophthal Soc U k 39 245
- 5 Chisholm I A Bronte Stewart J & Foulds W S (1967) Hydroxocobalamin ver sus Cyanocobalamin in the Treatment of Tobacco Amblyopia Lancet 2 450
- 6 Cox J (1960) Colour Vision Defects Acquired in Diseases of the Eye Brit J Oph thol Optics 17 195
- 7 Crone R A (1961) Quantitative Diagnosis of Defective Colour Vision Amer J Ophthal 52 995
- 8 Farnsworth D (1943) The Farnsworth Munsell Hundred Hue and dichotomous tests for colour vision J Opt. Soc Amer 33 563
- 9 Foulds W S Chisholm I A Bronte Stewart J & Wilson T M (1969) Vitamin B12 Absorption in Tobacco Amblyopia Brit J Ophthal 53 593
- 10 Foulds W S Chisholm I A Bronte Stewart J & Wilson T M (1969b) Cyanide Induced Optic Neuropathy Ophthalmologica Addit 158 350
- 11 François J & Verriest G (1961) An Acquired Deficiency of Colour Vision Vision Res 1 201
- 12 Galeowski (1883) Des Troubles Visuels Consecutifs a l'abus de Tabac Rec dupht. 4 677
- 13 Grunow A (1897) Ueber die Intoxications Amblyopie Arch f Ophth 39 1
- 14 Heaton J M McCormick A J & Freeman A G (1958) Tobacco Amblyopia A Clinical Manifestation of Vitamin B12 Deficiency Lancet 2 286
- 15 Ishihara S (1959) Tests for Colour Blindness 14th Ed Tokyo Japan.
- 16 Kollmer H (1910) Die Störungen des Farbensinnes Ihre klinische Bedeutung und ihre Diagnose Jarger Berlin
- 17 Lakowski R (1968) The Farnsworth Munsell Hundred Hue Test Ophthalmic Op tician 8 862
- 18 Lakowski R (1959) Age and Colour Vision, Advancement of Science 15 281
- 19 Lau F W (1951) Standardisation of Reading Types Brit J Ophthal 35 165
- 20 Lau F W (1951) Reading Types Brit J Ophthal 36 659
- 21 Phillips C J Anley R G Van Peborgh P Watson Williams E J & Bottomley I C (1968) Vitamin B12 Content of Aqueous Humour Nature (Lond) 217 67
- 22 Piddell W J R (1936) The Early Stages of Tobacco Amblyopia Glas Med J 1 5 63
- 23 Ridley F (1959) The Contact Lens in Investigation and Treatment Trans Ophthal Soc U k 19 535

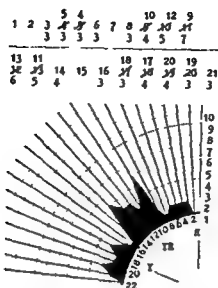


Fig 1
Specimen of Farnsworth Munsell 100 Hue score and profile

of 16 and 35 years (Lakowski 1958) After 55 years there is a rapid deterioration in the ability for fine colour discrimination which affects mainly yellow blue or violet blue green discrimination Red green discrimination remains fairly stable and is least affected by age Verriest (1963) demonstrated that in normal healthy subjects the error score for the Farnsworth Munsell Hundred Hue test increased in a positive manner with age from the age of 35 onwards At the age of 60 years he quotes a mean error score of 95 with an upper limit of 152 for men

Untreated Tobacco Amblyopia

A group of 65 patients of mean age 67 years was composed of 64 males and one female of whom 57 smoked pipe tobacco only 3 cigarettes only and 5 both The mean tobacco consumption of the group was 3.04 ± 1.44 ozs per week They were diagnosed as suffering from tobacco amblyopia after the criteria of Heaton *et al* (1958) The mean error score for the right eye of all patients for the Farnsworth Munsell Hundred Hue test was 732 ± 236 In an earlier communication (Chisholm 1969) it was suggested that in the case of error scores above 600 a mean of several test results be taken and below 600 a single test result would be sufficiently reliable Where possible this premise was adhered to A typical 100 Hue profile in untreated tobacco amblyopia shows depressed dis

pia The Farnsworth Munsell Hundred Hue profiles obtained in our series of cases show a depression of colour discrimination in most regions of the spectrum but with a predominant red/green loss. We have noticed also that with treatment the profile improves slowest in the red green area.

The mode of action of hydroxocobalamin in the treatment of this disease is as yet obscure. The degree of visual improvement with therapy suggests that the neuro retinal cells have been malfunctioning and on the removal or counter action of the toxic agent have undergone recovery. The pallor of the optic disc present initially did not alter on therapy.

The Farnsworth Munsell 100 Hue results are a sensitive index of visual function recovery and allow this to be followed quantitatively. The Farnsworth Munsell 100 Hue profiles do not establish whether tobacco amblyopia is a disease primarily of the optic nerve pathway or of the neuro retina as discussed by Schanz (1920) and Phillips *et al* (1968). The profiles obtained differ markedly from those obtained from Leber's Hereditary Optic Atrophy patients in whom the central visual acuity is also poor but the dyschromatopsia is characteristically of a red green loss.

Summary

A defect of colour discrimination is a consistent feature of tobacco amblyopia. In the untreated condition the defect takes the form of an irregular depression of colour discrimination in most regions of the spectrum. Poor colour discrimination was found to be related directly to poor visual acuity and increased age. Sixty patients were treated with parenteral hydroxocobalamin and continued smoking. Five patients stopped smoking as their only form of therapy. When the disease was associated with pernicious anaemia the rate of visual improvement was slower than that when diabetes was the associated condition. When there was no associated disease the rate of visual improvement with hydroxocobalamin was as good as that obtained when smoking was stopped.

Acknowledgement

We wish to record our thanks to the various Consulting Ophthalmologists of the Western Region (Scotland) who referred cases of tobacco amblyopia. We also thank Professor W. S. Foulds for the use of the facilities of the Fennell Institute. Mr G. Donald of the Medical Illustration Department, Western Infirmary for the illustrations and Mrs M. Revans for secretarial assistance. Doctor J. F. Adams, Southern General Hospital, carried out the vitamin B12 assays. Professor W. I. Card, Professor of Medi-

crimination in most regions of the spectrum (anarchic profile) with preferential loss in the red/green region

The response of these patients to the pseudo isochromatic plates of the Ishihara pattern (1959) was also examined. The results obtained were not as informative as those obtained by the Farnsworth Munsell Hundred Hue test. All patients showed a gross abnormality of colour vision, some patients being unable to identify the numeral on the first plate which is recognised by all congenital dichromats.

The best visual acuity (Snellen) of the right eye of all patients prior to treatment was converted to percentage visual acuity (Ridley 1959). The mean visual acuity was found to be 18% (equivalent to 6/36 Snellen) with a range 1.5%–100%. The near visual acuity was estimated using the notation laid down by the Faculty of Ophthalmologists (Law 1951–52) and similarly transposed to the percentage visual acuity scale. The near acuities lay within the range 8% to 64% with a mean at 20.75% (< N18 at 15 inches). No significant difference could be demonstrated between the mean distance acuity and near acuity ($t = 0.5$; $n = 116$; $p > 0.1$).

When the Farnsworth Munsell Hundred Hue error score was compared with the distance percentage visual acuity, a significant positive correlation was obtained ($r = +0.402$; $n = 62$; $p < 0.001$). A correlation was also obtained when the Farnsworth Munsell Hundred Hue error score was compared with the patient age ($r = +0.325$; $n = 62$; $p < 0.01$) (Fig. 2).

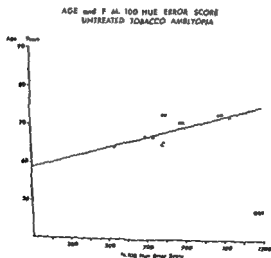


Fig. 2

Correlation of Age and Farnsworth Munsell 100 Hue showing regression line in untreated tobacco amblyopia

chine in relation to Mathematics and Computing gave helpful advice on the statistical evaluation of the results. Financial aid for this investigation was provided by the Machine in relation to Mathematics and Computing gave helpful advice on the statistical Research Council and Glaxo Ltd.

References

- 1 Bouin C & Coscas G (1966) Etude Statistique et Analytique de 164 cas de Nevrite Optique Alcoolique tabagique. *Ann Oculist* 199 925
- 2 British Standard 950 part 1 (1967) Artificial Daylight for the Assessment of Colour. British Standards Institution, London.
- 3 Carroll F D (1956) Toxic Amblyopia. *Trans Amer Acad Ophth* 60 74
- 4 Chisholm I A (1969) An Evaluation of the Farnsworth Munsell Hundred Hue test as a Clinical Trial in the Investigation and Management of Ocular Neurological Deficit. *Trans Ophthal Soc U K* 89 745
- 5 Chisholm I A, Bronte Stewart J & Foulds W S (1967) Hydroxocobalamin versus Cyanocobalamin in the Treatment of Tobacco Amblyopia. *Lancet* 9 450
- 6 Cox J (1960) Colour Vision Defects Acquired in Diseases of the Eye. *Brit J Physiol Optics* 17 195
- 7 Crone R A (1961) Quantitative Diagnosis of Defective Colour Vision. *Amer J Ophthal* 51 998
- 8 Farnsworth D (1943) The Farnsworth Munsell Hundred Hue and dichotomous tests for colour vision. *J Opt Soc Amer* 33 568
- 9 Foulds W S, Chisholm I A, Bronte Stewart J & Wilson T M (1969) Vitamin B₁₂ Absorption in Tobacco Amblyopia. *Brit J Ophthal* 53 393
- 10 Foulds W S, Chisholm I A, Bronte Stewart J & Wilson T M (1969b) Cyanide Induced Optic Neuropathy. *Ophthalmologica* 158 370
- 11 François J & Verriest G (1961) An Acquired Deficiency of Colour Vision. *Vision Res* 1 201
- 12 Galeowski (1853) Des Troubles Visuels Consécutifs à l'abus de Tabac. *Rec d'ophth* 4 677
- 13 Goenowa A (1892) Ueber die Intoxications Amblyopie. *Arch f Ophth* 35 1
- 14 Heaton J M, McCormick A J A & Freeman A G (1958) Tobacco Amblyopia. A Clinical Manifestation of Vitamin B₁₂ Deficiency. *Lancet* 2 86
- 15 Ishihara S (1959) Tests for Colour Blindness. 14th Ed. Tokyo, Japan.
- 16 Kellner H (1913) Die Störungen des Farbensinnes Ihre klinische Bedeutung und ihre Diagnose. Harger, Berlin.
- 17 Lokowski R (1969) The Farnsworth Munsell Hundred Hue Test. *Ophthalmic Optician* 8 867
- 18 Lokowski R (1955) Age and Colour Vision. *Advancement of Science* 15 281
- 19 Low F W (1951) Standardisation of Reading Types. *Brit J Ophthal* 35 105
- 20 Low F W (1951) Reading Types. *Brit J Ophthal* 36 659
- 21 Phillips C I, Amley R G, Van Peabrogh P, Watson Williams E J & Bottomley A C (1968) Vitamin B₁₂ Content of Aqueous Humour. *Nature (Lond)* 217 67
- 22 Riddell W J B (1936) The Early Stages of Tobacco Amblyopia. *Glas Med J* 15 68
- 23 Ridley F (1959) The Contact Lens in Investigation and Treatment. *Trans Ophthal Soc U K* 9 533

Thygeson (1956) found 10 per cent to recover spontaneously while Laibson (1961) saw 24.5 per cent to be cured after placebo treatment alone. Burns found placebo and IDU to be equally effective in the treatment of chronic keratitis or relapses. Davidson obtained healing of dendritic keratitis in half of his patients within 14 days of instillation of 1 per cent gamma globulin which he himself regarded as a placebo.

The immediate success of a treatment (fading of the dendritic pattern and shadowy transformation on IDU treatment and decreasing ciliary congestion on steroid treatment) need not indicate a favourable response at the long view. To study the effect of the treatment given I have followed up just over 100 patients to compare the therapy with two of the parameters on which an evaluation of the therapeutic effect on the long view may be based namely the recurrence rate and the visual acuity at the time of the follow up.

Present investigations

The investigation comprised all the patients referred within a seven year period (1958-1964) to the Department of Ophthalmology Kommunehospitalet with dendritic keratitis i.e. a corneal affection presenting a typical dendritic pattern.

This characteristic disease was described as early as 1884 by the first professor of ophthalmology in Denmark Edmund Hansen Gruet (keratic ramific). No virus cultivation was performed to verify the herpetic affection the morphological picture being generally regarded as sufficiently specific to justify a diagnosis of herpetic keratitis.

Incidence

Within the seven year period 157 patients were seen who had had one or more attacks of dendritic keratitis i.e. 22.4 patients annually.

Several of these patients experienced renewed attacks within the seven year period. Thus a total of 287 attacks were recorded of which some repeated i.e. 41 attacks annually.

During the same period 6062 patients were admitted to the Ophthalmic Unit while 50270 were treated as out patients. Among these a total of 952 had keratitis of some kind or other. The recorded cases of dendritic keratitis constituted 1.96 of the total number with ophthalmic diseases.

Jonkers found herpetic keratitis to constitute 1/250 of all cases of ophthalmic diseases in Holland

The Department of Ophthalmology *Kommunehospitalet* serves a population of about 700 000. Only a certain proportion of herpetic keratitis cases are referred to the Ophthalmic Out Patient Department, a fairly large number being treated ambulatorily by ophthalmic medical practitioners. The incidence is accordingly much higher than that recorded in the present paper (59/1 million annually).

In the author's own practice within the same region on an average 10 cases have been recorded each year. This corresponds to about 500/1 million annually.

The series under review from an ophthalmic unit must be supposed to comprise in particular fairly severe cases, while milder cases often have been treated by ophthalmic medical practitioners.

Sex and Age

Males predominated definitely in this series, 93 males against 64 females (59 per cent males). Male preponderance has been encountered in all the series described. It is often even more pronounced than in the present (*Gundersen* 149 males against 75 females; *Thygeson* (1956) 135 males against 65 females; *Laibson* 72/28; *Jonkers* 154/37; *Sood* 97/53; *Gilles* 100/59).

The age incidence at first attack is shown in table I. A fairly large proportion of the cases are grouped within the first ten year period, with an equal representation of the two sexes. Another maximum within the age group of 40-50 years was due to preponderance of males. Males predominated in all age classes above 30.

The age distribution shows that the primary infection or an early relapse of

Table I
Dendritic keratitis: age and sex incidence, 151 cases

age	0	10	20	30	40	50	60	70	80
females	12	9	12	2	11	9	5	4	0
males	12	6	7	14	16	12	13	11	2
Total	24	15	19	16	27	21	18	15	2

- 24 Ross G I M (1952) Vitamin B12 Assay in Body Fluids Using *Euglena Gracilis* J Clin Path 5 250
- 25 Saraux H Labet R & Biais B (1966) Aspects Actuels de la Nervite Optique de l'ethylique Ann Ocul 199 943
- 26 Schanz F (1920) Zeitschrift f Augenh 43 73
- 27 Verriest G (1963) Further studies on acquired deficiency of colour discrimination J Opt Soc Amer 53 185

The equatorial region of both the anterior and posterior parts of the sclera revealed three types of small areas. They could produce higher or lower echo amplitudes than the control values or they could divert the sound beam to such extent as made it impossible to register the sound with the described movements of the ball.

The lens caused strong attenuation in the axially moving sound while the edges of the lens had much less effect in this respect. The edges could however cause a distinct change in the position of the sound beam and they could produce maxima and minima in the echo amplitude curves. Those two points of the optic nerve which were examined could either weaken or intensify the sound beam. Their echo amplitude curves showed maxima and minima.

The results of the experiments show that, depending on the relation between the sound beam and the tissue several kinds of changes may be observed. These include attenuation, intensification, reflection and refraction. Under certain conditions total reflection may be observed. The intensification of the sound field which is fairly small may be due to the focusing effect of the tissue or to an interference phenomenon caused by it. Examinations of the sound fields show that tissues may change the acoustic properties of various parts of any cross sections of the sound field so that they become quite different.

Summary

Pig eyes were used for an experimental investigation of the effect of the cornea, sclera, lens and optic nerve on the sound fields in the various relative positions of the sound beam and the tissues. Three different cross sections of the sound field were studied. When the sound travelled at right angles through the tissue either strong (the lens) or slight (the cornea and sclera) attenuation was observed. When the angle was increased to 30° also the amount of attenuation increased. When the sound hit the tissue at a 70° angle it was either reflected, attenuated or even intensified. The latter phenomenon is probably caused by a focusing effect of the tissue. Various tissues may make any cross sections of the sound field very irregular in strength and shape.

References

- Oksala A & Blok P. Der Einfluss von Linsen auf das Schallfeld. Experimentelle Untersuchungen mit Schweinelinsen. In *Diagnostica Ultrasonica in Ophthalmologia* ed by J Vanysek. Universita J E Purkyne Brno 1968 pp 185-197.
Oksala A & Hakkinen L. Der Einfluss der Augenhülle auf das Schallfeld. Experiment

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EXPERIMENTAL INVESTIGATIONS OF THE EFFECT OF VARIOUS PARTS OF THE EYE ON THE SOUND FIELD IN THE ULTRASONIC METHOD

BY

ARVO OKSALA

Earlier experimental investigations in which one cross section of the ultrasonic field was studied showed that different parts of the eye may considerably change the sound field. If the sound travels perpendicularly through the cornea and sclera it will become slightly attenuated (Oksala & Hakkinen 1968). When the sound passes the lens axially strong attenuation is observed (Oksala & Blok 1968).

If the sound meets the cornea and sclera at an approx. 30° angle its attenuation is clearly observed. When the angle is approx. 10° even a total reflection may be found (Oksala & Hakkinen 1969). If the sound passes the edges of the lens slantingly it will be both attenuated and refracted (Oksala & Blok 1968). If the sound beam hits the rear eye wall at a 10° angle its course may change because of refraction and possibly because of reflection too. The optic nerve may produce an absolute or relative acoustic shadow (Oksala & Nuranen 1970).

This study tries in another way to clarify experimentally the effects of the

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mic tonometry also offers accurate registration of the pulse synchronous changes in eye tension & the corneal indentation pulse. Normally the corneal indentation pulse amplitudes average a plunger movement of about 30 microns & 0.6 scale reading Schiötz. A repeated amplitude difference between the two eyes of 15% or more is considered a definite pathological finding (Horten 1940).

Clinically the method was applied to the following cases

Case 1 girl aged 14. Extensive cutaneous hemangiomas of face, upper part of truncus and extremities as shown in Fig. 1. Treated for epileptic attacks from the age of seven months. Right sided homonymous hemianopsia with macular sparing, left sided F.E.C. changes and calcifications in the occipital cortex as revealed by X ray examination. Psychological tests indicate a decreased capacity of learning. A rise in intraocular pressure was noted on the left side at the age of 14 years when the first dynamic tonometry examination was performed as listed in Table 1. She was treated with pilocarpine 4 times daily in left eye. At this time eye examination revealed distended episcleral vessels on both sides. Corneal diameters were within normal limits and the anterior chambers appeared normal with normal angles as judged by gonioscopy. The optic discs showed central physiological excavations and the fundi appeared normal.



Fig. 1
Case 1

above mentioned parts of the eye on the ultrasonic field. The investigation is based on the results of 3 cross sections of the same sound field.

Equipment, material and method of research

The model of the ultrasonic equipment was Kretztechnik 7000 and the measurements were registered with a Tektronix oscilloscope. The 7.5 Mc/2 mm transducer was unfocused. The amplification of the equipment was kept at the same level throughout the investigation.

For the measurement of the sound field a device was constructed where an SKF steel ball could be moved in three different directions beneath the transducer which had been fixed to a stand. The diameter of the steel ball was 1.5 mm and the ball itself worked as a reflector of sound. The position of the ball in respect to the transducer could be determined with an accuracy of 0.1 mm. The three cross sections of the sound field were obtained by moving the ball first through the sound field via the center of the transducer and then parallel to the first cross section on each side at a distance of 2 mm. The amplitudes of the echoes reflected by the ball could be drawn into echo amplitude curves. These amplitudes are proportional to the sound pressure at the corresponding points.

The material consisted of pig eyes. Different calottes were prepared: calottes formed by the cornea and the anterior part of the sclera; calottes of the posterior part of the eye with and without the optic nerve; and lenses with capsules. After the transducer and the ball had been immersed in water, the above mentioned parts of the eye were placed one after another on a copper wire rack between the transducer and the ball so that the copper wire lay outside the sound field. The distance between the transducer and the ball was 30 mm and from the transducer to the nearest point of the tissue 5 mm. Control fields were measured in water without the tissues.

When the effect of the cornea on the sound field was investigated, the sound was first directed perpendicularly to the center of the cornea and then towards its edge. With the sclera under examination, the sound was first directed to the vicinity of the limbus and then near the equator of the eye. When the effect of the scleral rear wall calotte on the sound field was examined, the sound first travelled perpendicularly via the center of the calotte and afterwards through its edges. While the lens was in the sound field, the sound first passed axially through the lens and then through its edges. The investigation of the optic nerve was first done at the papilla and then 3-4 mm further back. In the latter case an opening was made on the scleral calotte so that the sound hit only the optic nerve. Each phase was carried out with 20 different samples of the particular

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CORNEAL INDENTATION PULSE IN STURGE WEBER SYNDROME

BY

T FLAGE & I HORVEN

Sturge Weber syndrome is characterized by nevus of the skin angiomatous involvement of the meninges and brain epilepsy and often glaucoma (Walsh & Hoyt 1969)

Congenital glaucoma with buphthalmus is characteristic but glaucoma with later occurrence without buphthalmus is also seen. Histologic examination has shown angioma of the choroid to be present in a considerable proportion of eyes enucleated for glaucoma (Dunphy 1935). Most of the angiomas are flat lesions involving the entire choroid. Clinically the angiomas may constitute a choroidal tumor but in most cases the angioma is not visible by ordinary ophthalmoscopy.

It is known that the blood volume of the choroidal system is about 37 times that of the retinal system (Chao P & Bettman J 1957). Accordingly hemangiomas of the choroid should be of major importance for the pulse synchronous changes in intraocular pressure by yielding an increase in the pulsatile part of the choroidal vascular bed with a corresponding increase in the corneal indentation pulse amplitudes.

Material and Methods

Dynamic tonometry is performed by use of an improved electronic tonometer as described by Horven (1968). In addition to record the eye tension per se dynamic

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part of the eye. All investigations were made in a temperature of $+20^{\circ}\text{C}$. All measurements took place in the far field of the transducer.

Results

1 Cornea

When the sound travelled perpendicularly through the center of the cornea all three cross sections of the sound field were very similar to the control measurements made in water. The highest amplitude was however in most cases about 1 db lower than in water control. When the sound traversed the edges of the cornea 16 cases showed cross section curves which were 2-3 db lower than the control curves but in 4 cases they were 2-3 db higher than the control curves. The edges of the cornea usually caused a narrowing in the sound field and 2 maxima and one minimum could often be observed in the curves. Fig. 1 represents the result of such a measurement. The three cross sections of the sound field measured in water control can be seen at the bottom on the left. In the middle one can see three cross sections obtained from the sound field when the sound travelled at right angles through the center of the cornea and top right we have the curves from the edges of the cornea. They are higher than the control curves and show two maxima and one minimum.

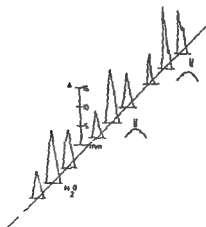


Fig. 1

Three cross sections curves obtained through the edges of the cornea (top right) are higher than the other curves

sided buphthalmus with a corneal diameter of 13 mm. The disc was cupped but otherwise the fundus appeared normal. The left eye revealed normal findings and so did E.E.G. and X-ray examination of the skull.

The glaucoma in the right eye could not be controlled medically; an iridectomy procedure was therefore performed on October 7th 1969. Dynamic tonometry results obtained before and after the surgical procedure are at increased and normal intraocular pressure levels are presented in Table 1. Fig. 3 gives the preoperative dynamic tonometry results which demonstrate a striking increase in corneal indentation pulse amplitudes of right eye.

Discussion

The corneal indentation pulse reflects primarily a pulse synchronous change in intraocular pressure initiated by the excess of blood which enters the eye in systole. If the pulsatile vascular bed of the eye increases the corneal indentation pulse amplitudes will yield a corresponding increase as may be demonstrated in eyes harboring malignant melanomas (Horven 1969).

An increase of corneal indentation pulse amplitudes is also seen in carotid cavernous fistula (Boyes & Ralph 1954) during pain attacks of cluster headache (Broch *et al.* 1970) and in glaucomatous or experimentally induced ocular hypertension (Horven 1970).

In the two cases of Sturge Weber syndrome presented above dynamic tonometry was performed before and after treatment at hypertensive and normotensive levels of intraocular pressure. At both occasions a marked increase in corneal indentation pulse amplitudes was found in the affected eyes. As this in



Fig. 3

Dynamic tonometry from Case 2 preoperative recording. The first part of the curve demonstrates the high intraocular pressure in the right eye. The second part demonstrates the increase of the corneal indentation pulse amplitudes of the right eye. (d = right eye; s = left eye)

2 The anterior part of the sclera

The sound travelled through the sclera first near the limbus and then near the equator. In the former case all cross section curves showed a lowering by 5–10 db in comparison with the control curves. In the latter situation one could, if one wanted to, find near the equator scleral areas which caused in the highest amplitude either a strong fall or a rise (>10 db) or a reflection of the sound beam to such extent that it could not be found with the above mentioned movements of the ball. These three spots of the sclera were all situated near one another. At the same time some maxima and minima appeared and in many cases a transition of the sound beam. The latter phenomenon was due to reflection.

Fig 2 shows the distinct lowering in the amplitudes caused by the equatorial area of the sclera and the minima and maxima as well as the transition of the beam. In Fig 3 one can see a narrowing in the sound beam caused by a corresponding area of the sclera, the maxima and minima and in this case a strong rise in the amplitudes of all three cross sections.

3 The posterior part of the sclera

When the sound passed the center of the calotte at right angles the cross section curves were very much like the control curves but mostly 1–2 db lower than them. The edges of the calotte on the other hand revealed spots which produced either a distinct rise or a fall (approx. 5–10 db) in the highest ampli-

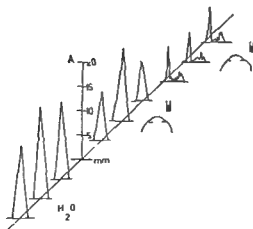


Fig 2

Three cross sections curves obtained through the equatorial area of the sclera (top right) are distinctly lower and more irregular than the other curves

Table I

Intraocular pressure and corneal indentation pulse amplitudes (μ) in two cases of Sturge Weber syndrome

Case No	Date	Treatment	Intraocular pressure in mm Hg (P_o)		Corneal indentation pulse amplitudes		% $\left(\frac{P}{100} \times N\right)$
			right	left	right	left	
1	Dec 13 1967	Before	20.6	34.5	45	90	200
	Jan 31 1968	After	18.9	12.2	52	88	169
2	Oct 2 1969	Before	41.4	13.4	60	16	375
	Nov 3 1969	After	18.9	15.9	16	10	160

by ophthalmoscopy. Under pilocarpine treatment which controlled the glaucoma on the left eye a second dynamic tonometry examination was performed as shown in Fig 2. The first dynamic tonometry examination performed when the intraocular pressure was pathologically increased on the left side demonstrated a marked difference in corneal indentation pulse amplitudes of the two eyes reading 45 microns on the right eye and 90 microns on the left (Table I). This difference was still present at the second dynamic tonometry examination which was performed at a normal intraocular pressure on the left side which proves that the increased amplitudes on the left eye are not primarily caused by a difference in eye tension levels on the two sides.

Case 2 boy aged 7. Cutaneous hemangiomas in upper right side of face in the region supplied by the first and second division of the trigeminal nerve. He is lefthanded and had some difficulties in learning to pronounce words. Right

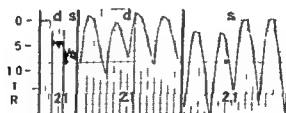


Fig 2

Dynamic tonometry from Case 1 after control of her glaucoma. The first part of the curve demonstrates a lower intraocular pressure in the left eye. The second part demonstrates the increased corneal indentation pulse amplitudes of the left eye. (d = right eye s = left eye)

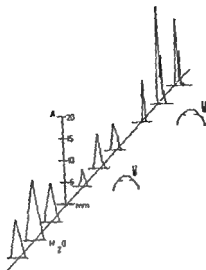


Fig 5

Cross sections obtained under similar conditions as the ones in Fig 2. In this case when the sound has traversed the sclera near the equator the curves are however higher and narrower than at the control examination.

tude when compared with the control curve as well as some maxima and minima. If so wanted one could at this examination too find near the edge of the calotte a small area which diverted the direction of the sound so much that it could not be found with the described movements of the ball. Fig 4 represents the results of an examination in which the three cross section curves at the top on the right are distinctly lower than the rest of the curves.

4. The lens

When the sound travelled axially through the lens the curves were approx 25-30 db lower than the control curves. When the examination was made through the edges of the lens the echo amplitudes that were registered were lower than in the control test but higher than at the axial examination. Fig 5 shows the results in one lens. When the sound traversed the lens axially the curves were very low while the edges produced distinctly higher echo amplitudes than the axial examination. The edges of the lens may cause the appearance of clear maxima and minima as well as a transition in the position of the beam due to the refraction.

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TREATMENT OF THE POSTOPERATIVE HYPOTONY SYNDROME

(Preliminary Report)

BY

RAGNAR TÖRNQUIST

The hypotony associated with shallow anterior chamber and choroidal detachment which may follow operations for cataract or glaucoma is usually caused by an external fistula (Meiler). Even if this complication develops some time (weeks or months) after the operation the explanation is the same. The rational therapy is to close the fistula and this is usually successful. Great emphasis is laid on the importance of the fluorescein test (Seidel's sign) for localisation of the fistula.

According to Hagen if the fluorescein test is negative there may still be a microfistula. Such cases may be more difficult to treat but in one case which followed Stallard's iridencleisis Rostengren obtained an immediate effect by the application of a silicone plomb over the site of the operation.

At the Eye Clinic in Örebro the same therapy has been used successfully in the cases of two patients.

Case Reports

1. A male born 1887 who since 1964 had been treated for glaucoma simplex of both eyes. In 1965 a thrombosis of the central retinal vein developed in the left eye. It was followed by clouding of the lens and marked reduction of vision. On 29th September

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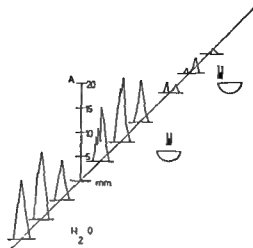


Fig 4

Cross sections curves when the sound passes through the posterior calotte of the sclera. Examination revealed a point near the equator which considerably lowered the echo amplitudes in comparison with the control values.

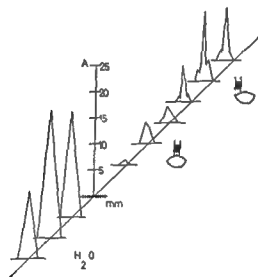


Fig 5

Cross sections of the sound field with the sound passing first axially through the lens and then through its edges. Axial attenuation is quite strong.

5 The optic nerve

The examination was made at two different points: the sound either passed the center of the calotte and pierced the papilla, or it travelled through the opening

crease was present also at normal levels of intraocular pressure it may not be fully explained by the initial ocular hypertension. It is therefore presumed that the increase in corneal indentation pulse amplitudes observed in these cases should mainly be explained by an increase of the choroidal pulsatile vascular bed. The existence of choroidal angiomas in these cases are most likely even if such were not seen by ordinary ophthalmoscopy.

Summary

Dynamic tonometry is presented as an easy way to prove ocular angiomatous involvement in patients with Sturge Weber syndrome.

References

- Boyes T L & Ralph F T: Carotid cavernous fistula. *Amer J Ophthal* 3: 262-266 1954
- Broch A *et al*: Studies on cerebral and ocular circulation in a patient with cluster headache. *Headache* 10: 1-8 1970
- Chao P & Bettman J: The relative volume of blood in the choroid and retina abstracted. *Amer J Ophthal* 43: 294 1957
- Dunphy E B: Glaucoma accompanying nevus flammeus. *Amer J Ophthal* 18: 69-714 1935
- Horven I: Dynamic tonometry I. The dynamic tonometer. *Acta Ophthal (Abh)* 46: 1218-1221 1968
- Horven I: Dynamic tonometry and choroidal melanoma. A new diagnostic approach. *Arch Ophthal* 82: 440-445 1969
- Horven I: Dynamic tonometry III. The corneal indentation pulse in normal and glaucomatous eyes. *Acta Ophthal (Abh)* 48: 39-58 1970
- Walsh F B & Hoyt W F: *Clinical Neuro Ophthalmology*. Third Edition. The Williams & Wilkins Company, Baltimore 1969

made on the sclera and hit the optic nerve 3-4 mm further back. In the former position the curves became 10-15 db lower than the control curves in 6 measurements out of a total of 20 in one measurement they were 2 db higher and in 13 measurements they were almost the same as the control values. In the latter position the curves were in 3 cases approx 10 db lower and in 17 cases 2-5 db higher than the control curves. All curves showed maxima and minima. Fig 6 shows how the area of the papilla causes a distinct fall in the intensity of the sound field while the part of the optic nerve which is further back intensifies the sound field.

Comments

If the sound passes perpendicularly through the calotte of the cornea and sclera the cross section curves of the sound fields show only slight changes when compared with the control curves. They may become somewhat lower and narrower. When the sound travels through the cornea and sclera at an approx 30° angle there is usually a greater fall in the curves with some maxima and minima. While cornea alone was the object of study the curves were found to be higher than the control values in four cases.

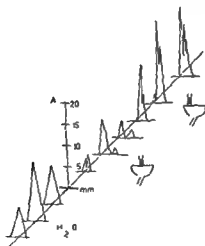


Fig 6

Cross sections when the sound passes through the optic nerve first at the papilla and then 3-4 mm further back. In the former case considerable attenuation was observed. In the latter case the echo amplitudes are higher than at the control examination.

Discussion

The postoperative hypotony syndrome has a tendency to resolve spontaneously after varying intervals. Assessment of the efficacy of various therapeutic measures is therefore difficult. Many methods of treatment have been described (mydriatics, miotics, carbonic anhydrase inhibitors, pressure bandaging, etc.). Good results have been ascribed to most of these measures. The value of the method described here is uncertain because of the only limited experiences. That the immediate effect has persisted for a considerable time in all cases implies that the procedure has been therapeutically effective.

Further studies of the effects of this method under different conditions as well as experimental work should make it possible to identify the pathogenesis of the postoperative hypotony syndrome. In particular the theories concerning the origins of the choroidal detachments are uncertain and merit further study.

References

- Hagen S. *Klin Monatsbl Augenheilk* 66: 161, 1921.
Meller J. v. Graefes *Arch Ophth* 80: 10, 1911.
Rosengren B. *Acta Ophth* in press.

The equatorial region of both the anterior and posterior parts of the sclera revealed three types of small areas. They could produce higher or lower echo amplitudes than the control values or they could divert the sound beam to such extent as made it impossible to register the sound with the described movements of the ball.

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The results of the experiments show that depending on the relation between the sound beam and the tissue several kinds of changes may be observed. These include attenuation, intensification, reflection and refraction. Under certain conditions total reflection may be observed. The intensification of the sound field which is fairly small may be due to the focusing effect of the tissue or to an interference phenomenon caused by it. Examinations of the sound fields show that tissues may change the acoustic properties of various parts of any cross sections of the sound field so that they become quite different.

Summary

Pig eyes were used for an experimental investigation of the effect of the cornea, sclera, lens and optic nerve on the sound fields in the various relative positions of the sound beam and the tissues. Three different cross sections of the sound field were studied. When the sound travelled at right angles through the tissue either strong (the lens) or slight (the cornea and sclera) attenuation was observed. When the angle was increased to 30° also the amount of attenuation increased. When the sound hit the tissue at a 70° angle it was either reflected, attenuated or even intensified. The latter phenomenon is probably caused by a focusing effect of the tissue. Various tissues may make any cross sections of the sound field very irregular in strength and shape.

References

- Oksala A & Blok P. Der Einfluss von Linsen auf das Schallfeld. Experimentelle Untersuchungen mit Schweinelinsen. In *Diagnostica Ultrasonica in Ophthalmologia* ed by J Vanysek. Universita J E Purkyne Brno 1969 pp 185-197.
- Oksala A & Haklinen L. Der Einfluss der Augenhülle auf das Schallfeld. Experimentelle Untersuchungen mit Schweineaugen. In *Diagnostica Ultrasonica in Ophthalmologia* ed by J Vanysek. Universita J E Purkyne Brno 1969 pp 197-204.

1968 a *cyclodialysis* was performed on the *right eye*. The postoperative course was complicated by hyphaema with markedly raised intraocular pressure. On 19th September irrigation of the anterior chamber was carried out and at the same time an *Elliott's trephination* was performed. The intraocular pressure was reduced to normal but because of increasing lens opacification it was necessary to perform an *intracapsular lens extraction* on 14th May 1969 (with *alpha chymotrypsin*). The postoperative course was free from complications. The visual acuity was 10 with correction on 20th November 1969.

On 16th January 1970 there developed spontaneously a painful and rapid deterioration of the vision of the *right eye*. On examination three days later the vision was reduced to counting fingers at three metres. The anterior chamber was very shallow. The subconjunctival fistulation following the trephine operation seemed to be functioning well but no external fistula through the conjunctiva was seen. Large choroidal detachments were seen at the periphery of the fundus and the intraocular pressure was very low.

On 26th January a silicone plomb (silastic) was applied on the conjunctiva over the trephine opening in the sclera. Pressure was achieved by stretching the plomb before the episcleral sutures were tied. Four to five hours later the intraocular pressure had risen to 42 mmHg and therefore the tension of the plomb was slightly reduced. Two days later the anterior chamber was still very shallow and the intraocular pressure was 24 mmHg. The silicone plomb loosened spontaneously and was therefore removed on 29th January. On 3rd February the anterior chamber appeared to be of normal depth and about one week later the choroidal detachments had completely disappeared. On examination on 15th April the visual acuity was 0.7 with correction. The intraocular pressure was 14 mm Hg. The anterior chamber was reformed and there was no choroidal detachment.

2 A woman born 1906. At a routine refraction on 4th March 1970 raised intraocular pressure in both eyes was found. The anterior chamber of each eye was rather shallow. Gonioscopy revealed a narrow chamber angle in each eye (0-1 degree). Tonography showed C of the right eye to be 0.13 and C of the left eye to be 0.15. The intraocular pressure was not satisfactorily controlled with medical therapy and on 10th March 1970 a *sclerectomy* was performed on the *right eye*. Postoperatively a widespread choroidal detachment developed and the anterior chamber became more shallow. As the pressure in the *left eye* was not satisfactorily controlled with medical therapy a *sclerectomy* was performed on this eye on 24th March 1970. In this eye also a large choroidal detachment developed and the anterior chamber became completely lost. There was marked hypotony of both eyes. No fistula through the conjunctiva could be demonstrated. As the condition appeared to be stationary on 9th April 1970 an *anterior sclerotomy and injection of air into the anterior chamber* was performed on the *left eye* and on 16th April 1970 the same operation was performed on the *right eye*. Only a transient improvement was obtained and several days later the condition was unchanged. On 28th April 1970 a silicone plomb was applied to the *left eye* over the conjunctiva covering the scleral fistula. The anterior chamber reformed at the time of the operation and the choroidal detachment disappeared after a few days. On 5th May the plomb was removed. The same operation was performed on the *right eye* on 5th May 1970 and the anterior chamber deepened somewhat but the choroidal detachment did not disappear. The plomb appeared to be in correctly placed and therefore a further operation was performed on 11th May 1970 and a larger soft silicone plomb was applied over a greater area. The anterior chamber returned after a few days and the choroidal detachments disappeared completely.

- telle Untersuchungen mit Schweintaugen. In *Diagnostica Ultrasonica in Ophthalmologica* ed by J Vanysek Universita J E Purkyně Brno 1968 pp 192-206
- Oksala A & Hukkinen L. Experimental studies of the behavior of ultrasound in the sclera and cornea. In *Ophthalmic Ultrasound* ed by Gitter Keeney Sarin and Meyer Mosby Saint Louis 1969 pp 59-64
- Oksala A & Nuuranen A. Experimentelle Untersuchungen über den Einfluss der hinteren Augenteile auf das Schallfeld. Kongress Bericht SIDUO III Wien 1969. In print

ces occurred in only one patient. One year previously this patient had sustained severe cranial injury. Four hours after the encephalography transient blindness occurred. The X rays showed bilateral cortical atrophy. Nothing is stated about the aqueduct or the 4th ventricle.

In 1954 Reese (1) reported a series of 16 patients with bilateral homonymous hemianopsia in 3 of whom the blindness had arisen in connection with ventriculography. The diagnoses had been hypertension with severe headache, craniopharyngioma and increased intracranial pressure of unknown aetiology. Reese was the first to point out the possible pathogenetic role of the posterior cerebral arteries. Incarceration of these vessels in the tentorial notch owing to a difference in pressure above and below the *tentorium cerebelli* or possible spasms in the vessels might explain the blindness as being of cortical nature. In further support of this theory Reese reported a case of bilateral homonymous hemianopsia in which autopsy showed the cause to be thrombosis in the basilar artery extending into both posterior cerebral arteries associated with bilateral cortical necrosis of the occipital lobes. This not uncommon post mortem finding had previously been described by Moore & Stern (6) (1938).

Rinaldi *et al* (8) (1961) described 5 patients who developed cortical visual disturbances after ventriculography and/or ventricular decompression.

In 3 patients with pinealoma or tumour of the 3rd ventricle a Torkildsen drain was inserted after the ventriculography. All developed lasting blindness with preserved pupillary reaction and two also Anton's syndrome. Two of the patients who died 2 months and 1 year later came to autopsy and in both cases the visual cortex was found to be normal grossly as well as microscopically. One patient had a tumour in the 4th ventricle but in this case (a girl aged 4 years) the blindness was transient. Three days after the operation perception of light had returned and another 17 days later vision was restored.

In these 4 patients the visual loss may have been due to incarceration.

The 5th patient had metastases from a malignant melanoma with symptoms of massive incarceration. In this case autopsy revealed cortical infarction in both occipital lobes.

Rinaldi's 5 patients differ from those mentioned above and from ours in having had operation in connection with the ventriculography. Therefore the ventriculography cannot be interpreted as the sole aetiological factor in the blindness.

Lossius (4) (1955) reported 3 cases of impaired visual acuity and homonymous quadrantic anopsia in the left lower quadrant following ventriculography. In all 3 cases the visual field defects subsided spontaneously.

Present Investigations

The author perused the records for 335 patients who had ventriculography in

ten was localized in the cornea while attacks of keratitis occurring later in adults may have been provoked by injuries at the place of work a fact which possibly accounts for the male preponderance

However only few patients gave a history of injury immediately before the eruption of herpes on the cornea

The age and sex incidence noticed corresponded fairly closely to that in Gundersen's series in which the age classes under 16 comprised 23 males and 23 females while of the patients above this age 126 were males and 52 females

Gilkes likewise found maximum of cases within the age group of 40-50 years while only few patients were under 10. Sood noticed preponderance of females in the age group under 10 years and preponderance of males in the group over 30. In Laibson's series the majority were in the forties

Seasons

Herpetic keratitis is often released by a cold influenza or the like. The attacks might be conceived to occur particularly often within certain seasons. The month of onset of each attack (both first attack and relapses) is recorded in table II in as far as the time of onset is known

The attacks are seen to have been fairly equally distributed over the whole year with no particular accumulation within the months where colds prevail. On the contrary the number was somewhat greater during the six summer months (136) than during the six winter months (90)

This result - no significant seasonal variations - contrasts with those of other workers. Thus Gundersen found the greatest number of cases in September and October. Jones in September. Brandt *et al* in spring. Laibson in January February and March and Schenk & Hummer (quoted by Jonkers) a similar pre dominance

Jonkers observed no seasonal variations

Table II

Numbers of herpetic keratitis attacks within the individual months 226 recorded attacks on an average 19 attacks per month

month	1	2	3	4	5	6	7	8	9	10	11	12
number of attacks	15	14	17	14	14	14	22	25	27	13	14	14

We may thus probably be justified in concluding that no seasonal variations exist

Follow-up

The follow up was in all cases carried out by the author himself. Of the total series of 157 patients 109 were followed up 27 had died at this time. Of these 21 would have been over 70 four in the 60ies and two in the 50ies at the time of the follow up if alive.

The remaining 21 (13 per cent of the total series) were not followed up because the address was unknown (3) the patient was away (6) admitted to another hospital (2) placed in a remand home (1) or failed to appear for examination (9).

The 109 patients followed up are described below.

Bilateral Cases

Herpetic keratitis is usually a unilateral affection and relapses occur in the same eye.

However in ten of the 109 the affection came on simultaneously in both eyes and in one case there was keratitis in one eye and recurrence in the contralateral eye. Most of the patients with bilateral keratitis were children (six were under 10).

Only one patient experienced considerable impairment of vision of both eyes (a man aged 55).

Gunderson found 1 per cent bilateral cases among 221 patients. *Laibson* 2 per cent (150 patients). *Sood* likewise 2 per cent (150 patients). *Thygeson* 9.5 per cent (200 patients). The 10 per cent bilateral cases in the present series is thus a high figure compared with those of previous statements.

Primary Herpetic Keratitis

Primary keratitis was a likely diagnosis in seven of the 109 cases (follicular conjunctivitis or vesicles on eyelid forehead nose or cheek simultaneously with first attack of herpetic keratitis). Four of these cases were bilateral.

Thygeson (1956) found 4.5 per cent primary cases.

Herpes of Lips

Recurrent herpes of the lips is often seen in patients with dendritic keratitis.

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BILATERAL HOMONYMOUS HEMIANOPSIA FOLLOWING VENTRICULOGRAPHY

BY

K E RASMUSSEN

Bilateral homonymous hemianopsia is taken to mean blindness showing hemianoptic nature in the course of its development or regression. In bilateral homonymous hemianopsia there is loss of both halves of the visual field in both eyes; in other words the patient is extremely amblyopic or totally blind.

This visual disturbance has been reported following ventriculography by several authors.

The first report was *Masson's* (5) from 1933. Among 100 consecutive cases of ventriculography he found 6 of temporary blindness. Four of these patients had intracranial tumours (3 had choked discs) and two had symptoms suggesting encephalitis.

In 3 of the patients with intracranial tumours several hours elapsed from the ventriculography until operation or puncture done to equalize the difference in pressure over the tentorium cerebelli. In these cases therefore there could have been incarceration from above with consequent circulatory disturbances in the visual cortex and visual pathways. In these cases the visual disturbances did not occur until 2-4 hours after the ventriculography while in the last of the patients with intracranial tumour the blindness developed after evacuation of only 2 ml cerebrospinal fluid before the injection of air (the same occurred in one of the patients with encephalitis). In this case and in the two patients with encephalitis the cause had to be interpreted as injury to the white matter around the collateral trigone.

Among 501 lumbar encephalographies *Masson* found that visual disturban

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Summary

Eight cases of bilateral homonymous hemianopsia were found following ventriculography on a material of 335 patients. In 5 of these cases the vision returned to normal in less than 10 days, in one it had been restored at follow up 11 months later while in 2 cases no improvement had occurred at discharge from hospital 1 and 2 months after the ventriculography.

References

- 1 Bodian M. Transient loss of vision following head trauma. *N Y St J Med* 64: 916-920 1964.
- 2 Ethelberg S and Jensen Viggo A. Obscurations and further time related paroxysmal disorders in intracranial tumors. *Archives Neurol Psychiat* 68: 140-149 1952.
- 3 Hoyt W F. Transient bilateral blurring of vision. Considerations of an episodic ischemic symptom of vertebral basilar insufficiency. *Arch Ophthal* 10: 746-751 1963.
- 4 Lossins H M. Transitory visual disturbances after ventriculography. *Acta Psychiatrica et Neurologica Scandinavica* 31: 81-86 1956.
- 5 Masson C B. The disturbances in vision and in visual fields after ventriculography. *Bull. neurol. Inst. N Y* 3: 190-209 1933.
- 6 Moore M T and Stern A. Vascular lesions in the brain stem and occipital lobe occurring in association with brain tumors. *Brain* 61: 70-98 1938.
- 7 Reese F M. Bilateral homonym hemianopsia. *Amer J Ophthal* 38 (part 1): 44-57 1954.
- 8 Rinaldi I, Botton J E and Troland C E. Cortical visual disturbances following ventriculography and/or ventricular decompression. *J Neurosurgery* 19: 568-576 1962.
- 9 Shellshear J L. A contribution to our knowledge of the arterial supply of the cerebral cortex in man. *Brain* 50: 236-253 1927.
- 10 Walsh F B. Clinical neuro ophthalmology. Baltimore: Williams & Wilkins Co. 2nd ed. XVI: 1294 pp (see pp 1104-1106) 1957.
- 11 Westby Reidar A and Dietrichson P. Insufficiency of the vertebral basilar arterial system. *Acta Ophthal* 41: 416-429 1963.
- 12 Wold A og Leira H. Temporær cortical blindhed efter blodnødsjokk. *Tidskrift for Den norske lægeforening* 84: 184-185 1964.

Two hours postoperatively she had no perception of light. Her pupils were dilated of equal size showing sluggish reaction to light. Only slight venous congestion no venous pulsation. Ophthalmoscopy otherwise unchanged.

On the day after the ventriculography the vision was finger counting at 2 m on both sides. The right pupil was smaller than the left both reacted to light the left more sluggishly than the right. Visual field for fingers. Left sided homonymous hemianopsia.

On the second day after the ventriculography no visual field defect was demonstrable and 9 days after the visual acuity in both eyes was 10. Pupils natural. Visual field for fingers showed no defects. Ophthalmoscopy unchanged.

Three months later blurred outlines of the discs without measurable prominence normal visual acuity and perimetry.

EEG 3 days prior to the ventriculography had shown a slightly abnormal curve with (4) 5.7 hz activity over both hemispheres without any definite difference between the two sides. Five hours after the ventriculography EEG showed a moderately abnormal curve with rather sparse alpha activity and quite some (3) 4.7 hz activity over both hemispheres without any difference between the sides and especially posteriorly over the hemispheres. Periodical bi occipital dampening. Normal occipital blocking on opening the eyes.

EEG 10 days after the ventriculography showed moderately severe abnormalities of the curve with sparse alpha activity over the right hemisphere and right sided preponderance in the temporo occipital regions of low frequent activity of (2½) 3.6 hz. On the basis of the EEG findings it could not be decided whether the lesion was in the cortex or in the white matter.

Case 2 (G 33310) Diagnosis Cerebral arteriosclerosis insufficiency of cerebral circulation

A woman aged 57 with arterial hypertension. Three years previously she had been admitted to an eye department with bilateral chronic chorioretinitis. At that time her blood pressure had been 210/110. Two weeks before her transfer to the neurosurgical department the patient had been admitted to a department of medicine after a subacute cerebral insult. She had right sided hemiplegia and aphasia but mentally she was awake and oriented. Blood pressure 210/110 - 140/100.

At the ophthalmological examination on admission the visual acuity had not been determined. Ophthalmoscopy showed old chorioretinitic changes but nothing else of note. Visual field for fingers natural.

Left sided carotid arteriography revealed delicate vessels throughout but no definite signs of space filling lesions. To rule out a parietal haematoma ventriculography was performed. While occipital burr holes were being made under local anaesthesia the blood pressure fell from 160/90 to 80/50. After injection of 1 resommin the blood pressure rose to 200 but gradually dropped again.

tics as the sole finding in women and children of families with Fabry's disease. In Spaeth & Frost's review the corneal opacities were described in 47 out of 51 cases.

Abnormalities III vessels in conjunctiva

The vascular abnormalities in the conjunctiva consists of small focal varicosities and ampulliform or saccular dilations and tortuosity of the vessels. Rahman found these changes in all males (8 patients) but could not demonstrate them in any females (6 patients). Spaeth & Frost noted that 26 out of 43 patients in their review showed similar findings. Colombi *et al* could not demonstrate conjunctival abnormalities in any of their 10 patients.

Abnormalities III the retinal vessels

These abnormalities are limited to the veins which may show angulation, tortuosity and haustrations. In their review of 77 cases including 12 of their own, Spaeth & Frost noted abnormal retinal vessels in 25 out of 46 cases. Colombi *et al* found that 2 out of 10 patients belonging to one family had similar retinal lesions.

Other ocular abnormalities

In addition to the above mentioned findings, periorbital oedema, oedema of the fundus, optic nerve atrophy and discrete stellate cataracts have occasionally been described in patients with Fabry's disease.

Present series

15 members of one family (family I) (fig. 1 and table I) were examined. 4 did not show any symptoms or signs of the disease, 1 female and 4 males did have the characteristic symptoms from the extremities, 3 females and 3 males had other general manifestations of the disease (from kidney, heart, lung and central nervous system). These findings are described in detail elsewhere (Christensen & Lou 1970).

The 7 females and 4 males with a history suggesting Fabry's disease all had characteristic skin and/or eye changes (figs. 2, 3, 4, 5 and 6). Five women presented skin lesions and in one of these, aged 30 years, these were the only sign. Five out of seven women showed pronounced corneal opacities while corneal changes could not be demonstrated in the other two. On the other hand, corneal opacities were the sole findings in two women aged 18 and 30 years respectively. Faint corneal opacities were seen in two males while this finding was question-

the Department of Neurosurgery G Århus Kommunehospital, during the 10 year period 1956-1966. In 172 cases the diagnosis was encephalitis and in 163 cerebral arteriosclerosis.

These two diagnostic groups were selected because none of the patients had undergone intracranial operations in connection with the ventriculography. Therefore the ventricular puncture may be considered a probable aetiological factor in bilateral homonymous hemianopsia.

Among the 335 patients studied, bilateral homonymous hemianopsia developed in only eight cases.

Case 1 (G 33224) Diagnosis: Chronic encephalitis

A 13-year old girl who had previously been in good health. Through the past 2 years she had been suffering from attacks of frontal pressure headache during the first 18 months accompanied by nausea and vomiting. For 3 months there had been brief episodes of blurred vision and diplopia especially when she was looking at the blackboard at school, transient dizziness, and blackening before the eyes when arising in the morning. General condition unaffected.

Neurological examination showed no abnormalities. Admitted because the ophthalmologist found choked discs.

Ophthalmological examination on admission. Visual acuity in both eyes 10. Pupils and ocular movements natural. Ophthalmoscopy. Small reddish discs surrounded by greyish tissue mainly on the nasal aspect. Prominence 1-2 dioptres. Veins dilated, faint venous pulsation. Perimetry 6/2000 for white and 10/2000 for red. Slightly enlarged blind spots.

To measure the intracranial pressure through 24 hours a drain was inserted into the lateral ventricle. Burr holes were made in the usual sites in the occipital region for ventriculography. On the right it was difficult to come on the ventricle. There was only a slightly elevated pressure and the inserted plastic drain was soon occluded. Therefore the drain was removed and reinserted on the left. Now the pressure in the ventricle was low and only a couple of ml cerebral fluid were evacuated. During the latter part of the procedure the patient was restless and complained of black spots before the eyes. A quarter of an hour later she was unable to see. Both pupils were dilated, the left one inactive to light while the right one gave a very faint direct reaction. The patient was agitated, slightly delirious. The pressure meter showed no excursion. Blood pressure 130/70 (as prior to the procedure).

The catheter was removed and ventriculography was done with puncture of both posterior horns. The ventricles were small. Otherwise the films showed normal appearances. No signs of space occupying lesions. The patient was believed to have encephalitis and the blindness was interpreted as a result of oedema so that concentrated type specified serum was administered. On this treatment the patient became entirely rational but remained blind.

The biochemical defect is a lack of a ceramide trihexoside cleaving enzyme (*Brady et al* 1967) leading to widespread accumulation of trihexose ceramide in the vessel walls and in the parenchyma of different organs mainly kidney and heart (*Sweeley & Khonsky* 1963 *Christensen Lou* 1966) Extensive pathological studies have been carried out by *Pompen et al* (1947), *Scriba* (1950) and *Jensen* (1966)

In males the first symptoms occur in childhood as attacks of severe pain peripherally in the limbs The pain is provoked by fever as well as by increased temperature in the surroundings Periods of fever and headache are prominent in many cases Skin and eye manifestations may often be present from childhood The course of the disease is often dominated by continuously deteriorating kidney function leading to death between 30 and 55 years of age Cerebral and cardiac symptoms may be present to a varying degree In females the symptoms generally occur at a later age are less prominent and the prognosis is usually good

The first feature of this disease to be noticed was the characteristic skin manifestations In males the cutaneous lesions generally appear about the age of 10-20 years In females the lesions are less frequent and less prominent and tend to occur at a later age The skin lesions are so frequent that *Wise et al* (1962) postulated that every patient with symptoms of Fabry's disease presents these lesions In recent years however it has become apparent that the skin lesions are not always present in Fabry's disease For example they may be lacking in young individuals and in females (*Jensen* 1966 *Colombi et al* 1968) The skin lesions consist of pin point to hemp seed sized brownish red often slightly elevated elements which do not become anaemic on pressure (Fig 3) The lesions often have a characteristic distribution being localized on the lower trunk genital region and upper thigh (Fig 2) Such skin manifestations are exclusively found in Fabry's disease (*Borch-Jorgensen & Borch-Jorgensen* 1965) In cases where skin lesions are lacking or doubtful eye manifestations may be present and of great value in the diagnosis

Steiner & Voerner described retinal vascular tortuosity in 1909 and aneurysmal vessels of the conjunctiva and corneal opacities were noted by *Weichsel* in 1925 *Rahman* (1963) and *Spaeth & Frost* (1965) have described these findings very thoroughly

Corneal opacities

The initial changes are described as a slight dust like haziness of the cornea The more advanced changes consist of whitish whorled streaks arranged in a vortex the center of the cornea The lesion is localized to the deep part of the corneal epithelium In *Rahman's* and in *Colombi et al's* materials all patients presented corneal changes *Colombi et al* (1967) have described corneal opaci-

EEG before the ventriculography had shown a slightly abnormal curve (6 ■ hz diffusely) Nine days later it showed a slightly to moderately abnormal curve (5 7 hz diffusely 7 hz in the right occipital region))

Histological diagnosis Mild meningitis mild chronic ganglion cell degeneration

Case 4 (C 16208) Diagnosis Meningitis cerebral metastases

A woman aged 20 who had been suffering from fatigue during the past 6 months and in whom a large abdominal tumour had been demonstrated two weeks before admission For the past 2 weeks bilateral peripheral facial palsy headache and vomiting as well as visual disturbances including diplopia.

Ophthalmological examination at admission Mild gaze paralysis of conjugate movement to the right Visual acuity in both eyes 10 Ophthalmoscopy and visual field for fingers normal

Ventriculography revealed normal ventricles and pressure (160 180 mm of water) 7 + 10 ml of slightly blood admixed to clear cerebrospinal fluid was tapped

Immediately after the ventriculography the patient complained of being unable to see The vision slowly returned and on the next day it had been fully restored The ventriculography showed normal appearances

The patient died 4 weeks later Autopsy showed acute meningo encephalitis and a metastasis in the right occipital pole immediately supero laterally to the calcarine fissure - from an ovarian carcinoma

Case 5 (G 18624) Diagnosis Encephalitis choked discs

A woman aged 24 who had two weeks before admission developed severe frontal occipital headache with a few vomitings and a temperature up to 38° C as well as some rigidity of the neck Three days later diplopia lasting for a couple of minutes

Ophthalmological examination at admission Visual acuity on both sides 10 Ophthalmoscopy Choked disc with a prominence of 1 dioptre on the right and less than 1 dioptre on the left Perimetry 10/2000 for white and red Normal

Neurological examination and electroencephalography failed to show any abnormalities

At ventriculography under local anaesthesia the ventricles were found to be normal and there were no signs of space filling lesions or distention Pressure 40 10 mm of water 21 + 2 ml of clear to slightly blood admixed cerebrospinal fluid was evacuated Blood pressure 120/80 constant during the procedure

After the ventriculography she went completely blind but her vision returned the same evening On the next day she complained of blurred vision Two days after the ventriculography ophthalmological examination showed a visual acuity of 10 in each eye Ophthalmoscopy was unchanged from prior

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to 140/80 Both ventricles were punctured without any complications and 1 ml fluid was tapped from the right side 3 ml from the left Pressure 100 mm of water Thereafter air was insufflated During the insufflation the patient became remote and later vomited As X rays showed that all the air was on the surface of the brain the ventricles were again punctured but as they now yielded only a few drops of cerebrospinal fluid no more air was insufflated

Now, the patient complained of being unable to see Visual field examination (with fingers) immediately after the ventriculography showed questionable left sided homonymous hemianopsia Eight hours later the patient was able to see hand movements at 1 m on the right and at 75 cm on the left Now there was definite left sided homonymous hemianopsia for fingers and a superior right sided quadrantic anopsia Ophthalmoscopy unchanged On the next day the visual acuity on the right was Hand movements at 1 m On the left Finger counting at 1 m Visual field defect unchanged

Two months later the appearances were unchanged Visual acuity on the right Finger counting at 1 m Left 2 m Visual field defect unchanged Left sided homonymous hemianopsia and right sided superior quadrantic anopsia

Case 3 (G 22075) Diagnosis Suspicion of cryptogenic encephalitis Choked discs

A woman aged 29 who had been having during the past 4 5 months brief episodes of blurred vision and obscurations up to several times daily initially in the left eye and during the past month also in the right Moreover there had been a period of one week with diffuse pressure headache without pressure exacerbations or other associated phenomena Ophthalmological examination showed on admission Visual acuity in both eyes 1 0 Ophthalmoscopy Discs hyperaemic prominence 3 4 dioptries Small haemorrhages on both discs Visual field for fingers normal

At ventriculography under local anaesthesia the pressure was 270 310 mm of water Blood pressure 140/85 constant during the procedure On both sides 11-12 ml first slightly blood admixed later clear cerebrospinal fluid was tapped A cortical biopsy was taken The X rays showed all the air on the surface During the ventriculography the patient complained of malaise and headache and at its completion she was blind (but with preserved perception of light)

On the following day vision began to return (not examined) Ophthalmological examination 3 days after the ventriculography Vision in both eyes less than 1 0 Ophthalmoscopy Unchanged from prior to the ventriculography Visual field for fingers natural

Four days later another ventriculography was performed but again failed This time there were no complaints of visual disturbances and subsequent ophthalmological examination showed unchanged condition

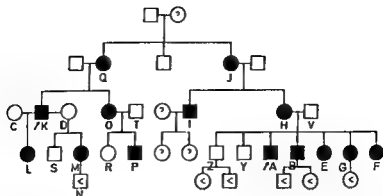


Fig. 1

Family I Information is lacking in the first generation of the pedigree. Hospital charts indicated the presence of Fabry's disease in the cases J, I and Q. K, O and H and all members of the next generation (except for two living in the U.S.A.) were examined by the authors and Fabry's disease was diagnosed in all cases except S, R, Z and Y which did not show any symptoms or signs of the disease. The last generation consists of small children and infants. At present it is impossible to determine whether they are involved or not.

able in the other two. In the last two cases the patients died from the systemic lesions of Fabry's disease and thus could not present for repeated examination.

In one woman 25 years of age abnormalities could be demonstrated in the conjunctival vessels and in another woman aged 57 years abnormalities were present in the retinal vessels. On the other hand abnormalities of the conjunctival vessels were seen in all males and of the retinal vessels in all males except one.

Comment and conclusion

The most frequent ocular manifestation in patients with symptoms of Fabry's disease is corneal opacities occurring with about equal incidence in males and females. Corneal opacities are often more pronounced in females than in males independent of the degree of skin and/or other manifestations of the disease.

Although similar corneal changes have been described in cases of chloroquine poisoning and in cornea verticillata, a corneal degeneration possibly unrelated to Fabry's disease, the corneal opacities are highly characteristic of Fabry's disease and are of special diagnostic value in the heterozygote females and young males.

In the present series all men and one woman with symptoms of Fabry's disease showed characteristic conjunctival vascular lesions. The occurrence of such conjunctival lesions in a woman has not been described previously. The finding

tigue and impairment of memory 11 days before admission suddenly severe occipital headache with blurred consciousness and incontinence of urine

On admission he showed rigidity of the neck a blood admixed cerebrospinal fluid mental deterioration but she was awake and fairly oriented as to her own data but not as to time and place

Ophthalmological examination at admission Vision in right eye 0.5 in left eye 0.67 Ophthalmoscopy Arteriosclerotic vessels but no other abnormalities Visual field for fingers normal

EEG revealed a moderately abnormal curve

On ventriculography the pressure was 50-70 mm of water Pronounced diffuse symmetrical atrophy of the ventricles Blood pressure 140/80 constant during the procedure

After the ventriculography the patient was torpid with sluggish reactions Therefore concentrated dry serum was administered and ventricular puncture was performed repeatedly

Gradually the patient awoke but was still severely deteriorated mentally and she gave an impression of being unable to see

20 days after the ventriculography the visual acuity could be determined At that time the vision on the right was perception of light and on the left hand movements in front of the eye Ophthalmoscopy Arteriosclerotic vessels and a small streaked haemorrhage at the right disc No other abnormalities

One month after the ventriculography the haemorrhage had disappeared Otherwise the ophthalmological findings were unchanged The visual field could not be determined

A cortical biopsy showed chronic meningo encephalitis

The patient was transferred to a nursing institution

Case 8 (G 16075) Diagnosis Suspicion of encephalitis

A woman aged 31 who had been suffering through 3 years from right sided frontal temporal headache orthostatic episodes on sudden changes in the position of the head and blackening before the eyes During the past 6 months decreasing visual acuity in the left eye

Ophthalmological examination showed visual acuity on the right to be 1.0 and on the left 0.5 Ophthalmoscopy Choked discs with a prominence of 2 dioptres Perimetry 10/2000 for white and red Normal

Neurological examination and electroencephalography failed to show any abnormalities

At ventriculography 6 + 1 ml of a blood admixed cerebrospinal fluid was tapped Pressure 260/340 mm of water The X rays showed no signs of dilatation of the ventricular system or of space occupying lesions.

After the ventriculography the patient complained of blurred and impaired vision in both eyes but finger counting was possible at 20 cm

Case (conf fig 1)	IL 18	IL 95	II 29	IM 30	IG 31	IO 49	III 57	II 17	IB 30	IA (died) 32	IK (died) 54
Age at latest examination (years)	+	+	+	-	+	+	+	+	+	+	+
Visible skin lesion	-	-	-	-	-	-	-	-	-	-	-
Vessel abnormal in fundus	+	+	+	+	+	+	+	+	+	+	+
Vessel abnormal in conj	+	+	+	+	+	+	+	+	+	+	+
Corneal opacities	+	+	+	+	+	+	+	+	+	+	+
Lye findings	+	+	+	+	+	+	+	+	+	+	+
Proteinuria	-	-	-	-	-	-	-	-	-	-	-
Azotaemia	-	-	-	-	-	-	-	-	-	-	-
Hypertension	-	-	-	-	-	-	-	-	-	-	-
ECG abnormalities	-	-	-	-	-	-	-	-	-	-	-
Cardiomegaly	-	-	-	-	-	-	-	-	-	-	-
Spontaneous pneumothorax	-	+	+	-	-	-	+	-	-	-	-
Febrile episodes	+	+	-	+	-	-	+	+	+	+	+
Fever and Heat provoked	+	+	+	+	+	+	+	+	+	+	+
Pains in extremities	+	+	+	+	+	+	+	+	+	+	+
Unilateral headache	+	+	+	+	+	+	+	+	+	+	+
Neurological deficits	+	+	+	+	+	+	+	+	+	+	+

+ Verified anamnestically and/or objectively - Disproved

A completely negative clinical examination and history was obtained in the cases S R 1 and 2 at the ages of 18 02 33 and 44 respectively (Fig 1)

to the ventriculography Visual field for fingers Left sided homonymous hemianopsia

Five days after the ventriculography there was left sided inferior quadrantic anopsia and 16 days later normal perimetry

At the ventriculography a piece of the cortex was removed for microscopic examination which showed normal appearances

Case 6 (G 24051) Diagnosis Encephalitis

A boy, aged 14 years with a familial predisposition to angioreticuloblastoma Admitted after some attacks in which he fell without losing consciousness or having convulsions

Ophthalmological examination at admission Visual acuity on the right 0.05 (squint amblyopia) on the left 1/25 Ophthalmoscopy normal Perimetry on the right 10/2000 for white Concentric narrowing suspicion of a defect in the upper right quadrant Red was not perceived Left eye 10/2000 for white and red Normal

Neurological examination and electroencephalography failed to show any abnormalities

At the ventriculography under local anaesthesia the ventricles were found to be normal without any signs of dilatation or space filling lesions Pressure 80-140 mm of water The blood pressure rose during the procedure from 125/100 to 160/100 but immediately after fell to 130/95 M + 13 ml of clear cerebrospinal fluid was evacuated

After the ventriculography the patient went blind On the following day he could perceive fingers On the third day after the ventriculography ophthalmological examination Visual acuity not determined mild chorioretinitis of the discs without measurable prominence Visual field for fingers Left sided homonymous hemianopsia

The patient was discharged 9 days later with unchanged left sided homonymous hemianopsia

At follow up admission 6 months later ophthalmological examination showed the visual acuity to be 0.05 on the right and 1/10 on the left Ophthalmoscopy visual field for fingers on the right and perimetry on the left 3/2000 for white Normal Perimetry with Goldmann's perimeter Inferior quadrantic defect which was unchanged 2 years later

At that time EEG showed a moderately abnormal curve with focal changes posteriorly on the right

Case 7 (G20688) Diagnosis Chronic encephalitis

A woman aged 62 who for the past 6 months had been suffering from decreasing visual acuity diplopia frontal pressure headache with dizziness fa



Fig 2

Pronounced skin lesions Patient IB) The lesions have a characteristic distribution being localized symmetrically predominantly on the lower trunk genital region and upper thigh



Fig 3

Close up view of skin lesion (Patient IB) showing the pin point to hemp seed sized dark(red) elevated elements

stitution must depend upon the length of time that the blood supply to the visual cortex is reduced and the underlying disease. However, as also emphasized by Walsh (10) it is usually good after ventriculography.

Although the named pathogenesis may in many cases afford a satisfactory explanation of the development of bilateral homonymous hemianopsia, several objections apply. The blindness does not arise in connection with stereotactic operations for parkinsonism, even though in this procedure far more air is insufflated than in ordinary ventriculography, so that the pressure over the tentorium cerebelli ought to be even more increased than in ordinary ventriculography. In the event of free flow between the supra- and infra-tentorial part of the ventricular system, it seems difficult to conceive why incarceration should arise. The free interval often reported between ventriculography and the appearance of visual disturbance makes it difficult to accept that bilateral homonymous hemianopsia should be due in all cases to incarceration in the tentorial notch with squeezing of the posterior cerebral arteries. Direct injury to the visual pathways or visual cortex, possibly with a haematoma, cannot be considered very likely considering the symmetrical visual impairment. However, in predisposed patients with an increased tendency to cerebral oedema, the puncture may easily be imagined to give rise to oedema around the visual pathways or possibly of the visual cortex. In 6 of the 8 present patients the diagnosis was encephalitis, and as these patients are known to have an increased tendency to oedema, the development of bilateral homonymous hemianopsia in these cases was perhaps due to oedema of the visual pathways around the trigone. In the patient with hypertension there is reason to believe that the fall of blood pressure from 160/90 to 80/50 has been the cause. In the patient with cerebral metastases there may possibly have been a question of incarceration, although this could not be proved at autopsy.

In 5 out of the 8 patients with bilateral homonymous hemianopsia, the vision returned to normal in less than 10 days; in one it had been restored at follow-up 6 months later, while in 2 no improvement had occurred at discharge 1 and 7 months after the ventriculography.

Among the 335 patients subjected to ventriculography there were, apart from the 8 with bilateral homonymous hemianopsia, another 7 with visual field defects (4 with unilateral homonymous hemianopsia and 3 with quadrantic anopsia) and 17 patients with other ocular symptoms, viz. blurred vision, fluttering before the eyes, spots before the eyes, micropsia, and in one case transient unilateral pupillary dilatation.

In the 11 patients with unilateral homonymous hemianopsia and homonymous quadrantic anopsia the prognosis was also good. A lasting defect was recorded in only one case. When first admitted this patient had hyperaemic discs with a prominence of 3-4 dioptres, and at follow-up 18 months later the discs were greyish white and atrophic.



Fig 4

Corneal opacities (Patient 1M) The opacities consist of whitish whorled streaks arranged in a vortex near the center of the cornea

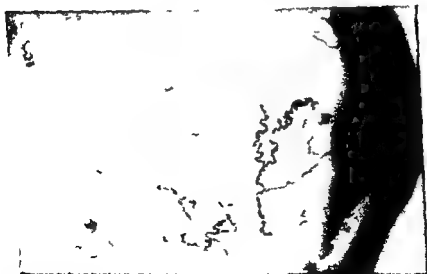


Fig 5

Vascular abnormalities in the conjunctiva (Patient 1B) The conjunctival vessels show some tortuosity and characteristic small focal varicosities and ampulliform and saccular dilations

Ophthalmological examination 2 days after the ventriculography showed the visual acuity to be 0.67 on the right and 0.33 on the left. Ophthalmoscopy unchanged. Visual field not determined.

Ophthalmological examination 10 days later showed the same appearances as prior to the ventriculography. Visual acuity 1.0 on the right and less than 0.67 on the left. Ophthalmoscopy unchanged. Visual field for fingers normal.

Discussion

The present study is a retrospective one and accordingly carries certain inaccuracies. The patients were not questioned particularly about ocular symptoms after the ventriculographies so that perhaps only the most pronounced cases have been recorded. Moreover the patients need not always have realized their blindness (Anton's syndrome) or have spontaneously mentioned their visual impairment.

Bilateral homonymous hemianopsia has been described also after arteriography following anoxia, head injuries, air emboli and vascular occlusion (1, 7, 12). The blindness may be the only finding although other ocular symptoms and systemic symptoms may co-exist depending upon the underlying disease (8, 11).

The aetiology of the sudden blindness following ventriculography is interpreted by most authors as cortical due to spasms or incarceration of the posterior cerebral arteries where they cross the edge of the tentorium cerebelli at the incisural level (3, 7, 8). The greater part of the visual cortex is supplied by these arteries. However its temporal part may also be supplied by a branch of the middle cerebral artery (9).

At the evacuation of cerebrospinal fluid and the subsequent insufflation of air into the ventricles it is imagined that a difference in pressure may arise between the supra- and infra-tentorial space with a risk of incarceration of the posterior cerebral arteries in the tentorial notch. The blindness often develops rapidly in relation to or immediately after the ventriculography. When vision returns there may be before complete restitution a transitional period of unilateral homonymous hemianopsia, a finding which might support the named pathogenesis (8).

Obscurations in the presence of elevation of intracranial pressure are interpreted in the same way as a consequence of intermittent disturbances of blood circulation in the visual cortex (2).

The fact that the cortical blindness may be accompanied by an impaired or abolished pupillary reaction to light must be assumed to be due to simultaneous spasms in the vessels supplying the brain stem. The prognosis as to visual re-

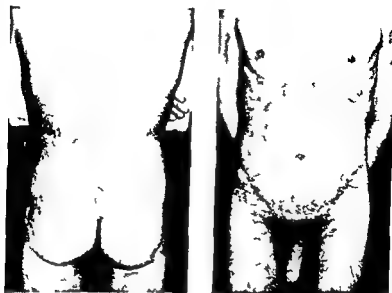


Fig 2

Pronounced skin lesions Patient IB) The lesions have a characteristic distribution being localized symmetrically predominantly on the lower trunk genital region and upper thigh

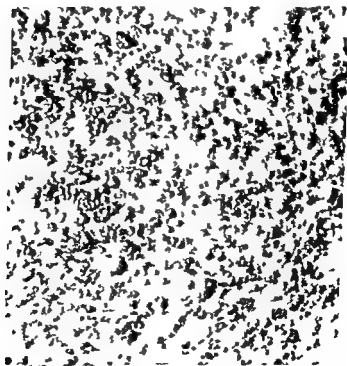


Fig 3

Close up view of skin lesion (Patient IB) showing the pin point to hemp seed sized dark(red) elevated elements

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THE VALUE OF OCULAR FINDINGS IN THE DIAGNOSIS OF ANGIOKERATOMA CORPORIS DIFFUSUM (FABRY'S DISEASE)

BY

HANS OLAV CHRISTENSEN LOU ERIK HEIDENSLEBEN
and HANS-WALTHER LARSEN

In the past decades the so called inborn errors of metabolism have attracted great interest. As a result our understanding of the underlying metabolic mechanisms have made great advances. Still however a rational therapy has ensued in only a few diseases. In the majority of metabolic diseases the physician has to content himself with making the diagnosis and giving genetic counselling.

Early diagnosis and genetic counselling are of particular importance in Fabry's disease as it is an X-linked recessive disorder with variable expressivity (Opitz et al. 1965) in which affected family members can in most cases reproduce. The first case reports on angiokeratoma corporis diffusum appeared in 1898 (Fabry, Anderson). Although the disease has been known since then it was not until 1958 that the first report of an affected woman appeared in the literature (Wallace). Our increased knowledge of the clinical manifestations and the genetic, biochemical and pathological mechanisms has resulted in the disease now being diagnosed more frequently. Up to 1960 only about 50 cases were reported but since then more than 50 additional cases have been described. The disease is not as rare as the literature might suggest since during the last few years Jensen and Christensen-Lou 1966 and Christensen-Lou 1970 found 24 cases in 4 families originating in the Copenhagen area.

heterozygote females and young males presenting only slight general manifestations

The presence of marked focal varicosities and ampulliform or saccular dilations of the conjunctival vessels together with tortuosity of the vessels may also be of great diagnostic value in this disease

Retinal vascular tortuosity is considered to be of no diagnostic value if not present together with other manifestations of the disease

Characteristic vascular lesions in the conjunctiva are described in a female for the first time

References

- Anderson W (1898) A case of angiokeratoma Brit J Dermat 0 113
- Borch Jørgensen M & B Borch Jørgensen (1963) Fabry's disease Dan med bull 12 157
- Brady R G & E Cal A M Bradley E Martenson A L Warshaw & L Laster (1961) Enzymatic defect in Fabry's disease New Engl J Med 26 1163
- Christensen Lou H O (1966) Fabry's disease a biochemical investigation Acta pathol et microbiol scand 68 339
- Christensen Lou H O (1970) Fabry's disease, a clinical and biochemical investigation (Thesis) (In prep)
- Colombi A A Kostyal R Brather F Cloor R Ma & H Thulen (1967) Angiokeratoma corporis diffusum - Fabry's disease Helv Med Acta 34 67
- Fabry J (1898) Ein Beitrag zur Kenntnis der Purpura haemorrhagica nodularis Arch Dermat u Syph 43 181
- Franceschetti A & A T Franceschetti (1968) Cornea verticillata et maladie de Fabry Path europ 3 369
- François J J Snacken & L Stockman (1963) Fabry's disease Path europ 3 347
- Jensen E (1966) On the pathology of angiokeratoma corporis diffusum (Fabry) Acta pathol et microbiol scand 68 313
- Jensen E & H O Christensen L u (1966) Fabry's sygdom Ugeskr for Læger Opit 3 M F C Stiles D Wise R R Race P Sanger C von Gemmingen R R Kierland E G Gross & W D Groot (1965) The genetics of angiokeratoma corporis diffusum Am J Hum Genet 17 375
- Pompen A W M M Ruster & H J G Wiers (1947) Angiokeratoma corporis diffusum (Fabry) Two autopsy reports Acta med scand 198 231
- Sahlman A V (1963) Ocular manifestations of hereditary dystopic lipidosis Arch ophthalmol 69 333
- Serila K (1970) Zur Pathogenese des Angiokeratoma corporis diffusum Fabry Verhändt deutsch Gesellsch Pathol 34 271
- Spath G L & P Frost (1963) Fabry's disease Arch ophthalmol 74 160
- Steier L & H Voerner (1909) Angiomatosis miliaris Deutsch Arch klin Med 96 103

Such recurrent attacks were reported by 56 per cent of our patients. Thygeson found herpes of the lips in no more than one third.

Recurrence Rate

Recurrence was noticed in 61 per cent of the 109 cases. Thus recurrence is seldom completely avoided.

In the whole series each patient had on an average 3.4 attacks, i.e. one first attack and 2.4 recurrences. There was no significant sex difference (males 3.6 attacks, females 3.1 attacks).

The number of attacks seemed to be the greatest in cases with first attack between the ages of 20 and 30 (on an average 7.8 attacks, 13 patients) against 3.5 attacks in 34 patients under 20. The frequency of attacks declines steadily after onset at the age of 30, presumably on account of decreasing observation periods.

All the attacks seen within the period of investigation and all the attacks stated in the past histories were included as such.

Intervals between Relapses

The time interval between the first and the second attack averaged 5.7 years (ranging from less than one year up to 47 years). Thus the patient can never feel safe against recurrence even after several years without such.

The interval is independent of the patient's age at the time of the first attack.

The interval between the first attack and the latest one recorded in cases with more than two attacks averaged 13.4 years (ranging from 2 to 30 years). Here too the interval was independent of the patient's age at the time of the first attack.

Observation Period

The figures given for recurrence rate and time interval between attacks depended largely on the length of the observation period.

The follow up was planned so as to obtain a sufficiently long observation period from the first attack. This period was never less than 5 years, often 5-12 years, the series having been collected from a seven year period. In 29 cases the observation period was still longer, these patients having had their first attack before the beginning of the proper period of investigation.

The observation period averaged 13 years.

The attempt to obtain a long observation period had, on the other hand, the

We may thus probably be justified in concluding that no seasonal variations exist

Follow up

The follow up was in all cases carried out by the author himself. Of the total series of 157 patients 109 were followed up 27 had died at this time. Of these 21 would have been over 70 four in the 60ies and two in the 50ies at the time of the follow up if alive.

The remaining 21 (13 per cent of the total series) were not followed up because the address was unknown (3) the patient was away (6) admitted to another hospital (2) placed in a remand home (1) or failed to appear for examination (9).

The 109 patients followed up are described below.

Bilateral Cases

Herpetic keratitis is usually a unilateral affection and relapses occur in the same eye.

However, in ten of the 109 the affection came on simultaneously in both eyes and in one case there was keratitis in one eye and recurrence in the contralateral eye. Most of the patients with bilateral keratitis were children (six were under 10).

Only one patient experienced considerable impairment of vision of both eyes (a man aged 55).

Gunderson found 1 per cent bilateral cases among 221 patients. Laibson 2 per cent (150 patients). Sood likewise 2 per cent (150 patients). Thygeson 9.5 per cent (200 patients). The 10 per cent bilateral cases in the present series is thus a high figure compared with those of previous statements.

Primary Herpetic Keratitis

Primary keratitis was a likely diagnosis in seven of the 109 cases (follicular conjunctivitis or vesicles on eyelid forehead nose or cheek simultaneously with first attack of herpetic keratitis). Four of these cases were bilateral.

Thygeson (1956) found 4.5 per cent primary cases.

Herpes of Lips

Recurrent herpes of the lips is often seen in patients with dendritic keratitis.



Fig 6

Left fundus of patient IH Some of the retinal veins show moderate tortuosity

of such lesions when pronounced must also be considered as highly characteristic of this disease

Retinal vascular abnormalities are especially seen in affected males In pronounced cases the abnormality is easily distinguished from normal vascular tortuosity In less pronounced cases however it is often difficult or even impossible to make this distinction

The present series confirms the diagnostic value of corneal opacities and conjunctival vascular abnormalities in Fabry's disease The occurrence of corneal opacities is of special diagnostic value in the heterozygote females and young males Paradoxically the corneal opacities were found to be more pronounced in the heterozygote females than in males even if the latter usually showed more severe general symptoms and signs

Summary

In this study of Fabry's disease 11 out of 15 members of one family presented symptoms and signs of this disorder

It is pointed out that corneal opacities are of great diagnostic value in both

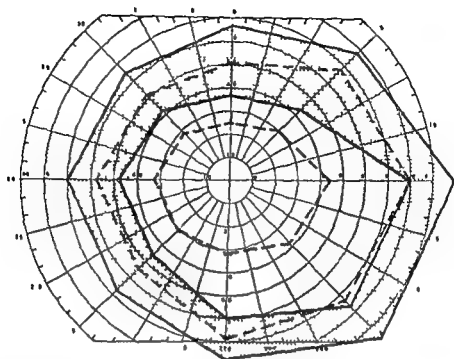


Fig 2

The variation observed with two different stimuli in kinetic perimetry obtained in a carefully standardized study of a large group of untrained normal subjects of different ages Redrawn from *Ferree et al*, 1931

The heavily stippled area illustrates the variation in perception thresholds for a stimulus subtending a visual angle of 1° at the eye The solid lines enclosing this area define the extreme limits (200 subjects) The lightly stippled area similarly illustrates the variation observed with a 0.17° stimulus in 150 subjects The broken lines define the corresponding extreme limits The rate of stimulus movement was not reported

experienced perimetrist who pays more attention to isopter shape than to size (*Traquair* 1939 *Lloyd* 1947 *Dubois Poulsen* 1952 *Harrington* 1964)

Isopter shapes

Rather than rigorously applying criteria of minimal permissible dimensions the experienced perimetrist thus aims to judge the shape of isopters This applies both to the primary distinction between normal and abnormal findings and to the further analysis of defective visual fields

The shapes of intermediary and peripheral isopters are most often loosely described as oval ovoid pear shaped etc The central isopters often appear more symmetrical but different authors diverge in opinion as to their shapes

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ON OBJECTIVE ANALYSIS IN KINETIC PERIMETRY

BY

L. FRISÉN

The examination of the visual fields is of recognized value in the detection and localization of eye and brain disorders. The methods of examination and the general understanding of their results have been improving for more than one hundred years. It is not certain, however, that the ability to tell normal results from abnormal has made similar progress: the primary pass or fail evaluation which determines the yield of the examination is still largely subjective and empirical. Although subjective evaluation may be appropriate in the differentiation between normal and grossly abnormal visual fields, it may be less suitable in the classification of borderline cases. A correct evaluation of such cases requires precise information as to what should be considered normal. This is at present mainly a matter of personal experience.

Objective and meaningful descriptions of normal findings should be of assistance in subjective evaluation and might even allow the use of objective testing methods. It is the aim of this paper to discuss various means of describing and analyzing the results of monocular kinetic perimetry, the most common form of examination, with particular reference to the shape of normal isopters.

The conceptions pertaining to the visual fields and their examination are in part vaguely defined. For this reason, the first part of this paper aims to present a concise outline of the subject matter.

some stating that they are circular others that they are elliptical or oval. Because of the successive change of isopter shapes from the center to the periphery within one and the same visual field and because of variation between and within subjects and examiners it is actually most difficult to define isopter shapes in unambiguous terms. It also appears that there have been no published attempts to assess objectively the shapes of isopters in the sense of describing the relationship between neighbouring points on the curves. On the contrary there is a prevalent attitude that the results of the visual field examination can only be judged subjectively (e.g. Harrington 1964). The evidence for this view does not appear to be available.

The theoretical derivation of isopter configurations from present knowledge of morphology and physiology appears impossible. The appalling number of factors involved is apparent already from the fact that a normal visual field finding presupposes integrity of the eye as well as the visual pathways and the visual cortex. Therefore approaches to the definition of isopter shapes are probably best directed to the actual findings of visual field examinations.

There are at least two apparently unexplored possibilities of improving the definition of normal isopter shapes. The one aims to reduce between subject variation, the other centres on a concept pertaining to shape characteristics.

Under standardized conditions of examination the larger part of the total variation in results emanates from between subject variation (Drance *et al* 1966). A reduction of this contribution to the variation would improve the conventional numerical definitions of normal isopter shapes by providing narrower limits of normality. One way of achieving this objective could be to correct for subject age. A decrease of isopter dimensions with increasing subject age has been demonstrated recently (Drance *et al* 1967, Fisher 1968). An older subject as a rule signals perception of a given stimulus closer to the point of fixation than does a younger one. The delay is attributable to increased reaction time, decreased attention, smaller pupillary area, decreased transmission through the ocular media, etc. changes which affect the dimensions of isopters without contributing information as to the state of the retina, the visual pathways or the visual cortex. However, such factors obviously are capable of variation also between subjects of one and the same age. Therefore their influence should not be dealt with primarily by correcting for subject age but by individual correction with their actual magnitude. This does not mean that the delay needs to be measured. It is in principle much simpler to correct for these between subject sources of variation by individually adjusting the strength of the stimulus so that isopters having standard features are obtained. It could be specified for instance that an intermediary isopter must always have say a temporal radius of 50 degrees of angle. As a rule then an older subject would need a stronger stimulus than a younger one to present an isopter of identical temporal radius. By using stimuli of individually appropriate strength it should

- Swcely C C & B Klionsky* (1963) Fabry's disease Classification as a sphingolipidosis and partial characterization of a novel glycolipid *J Biol Chem* 239 3148
- Wallace H J* (1958) Angiokeratoma corporis diffusum *Brit J Dermat* 70 354
- Weicksel J* (1925) Angiomatosis *Deutsch med Wochenschr* 51 898
- Wise D H J Wallace & E H Jellinek* (1962) Angiokeratoma corporis diffusum *Quart J med New Series* 31 177

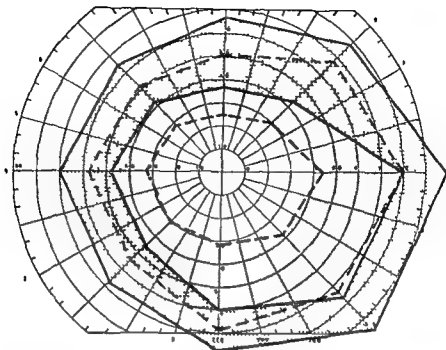


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Objective and meaningful descriptions of normal findings should be of assistance in subjective evaluation and might even allow the use of objective testing methods. It is the aim of this paper to discuss various means of describing and analyzing the results of monocular kinetic perimetry, the most common form of examination, with particular reference to the shape of normal isopters.

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plain the larger variation in threshold position in the upper part of the field (Fig 2)

The cartographic problem

Even the casual reader of geographical atlases has probably noticed the manifold possibilities of depicting a given geographical region. One and the same global area may assume quite different appearances in different maps. This is due to the fact that there exists no single cartographic projection that is able to represent without faults spherical surfaces in a plane. On the contrary, every cartographic projection involves characteristic distortions of linear, angular and/or areal relationships in varying extents across the map. Deformation is an unavoidable consequence of projection. This applies also to the standard cartographic projection of perimetry, the so called polar azimuthal equidistant projection. The deformational properties of this projection have been analysed recently on the basis of a model of the visual space (Frisen 1970). It will suffice to note the following characteristics of deformation here:

(I) Peripheral parts of an isopter outline are depicted on larger scales than parts lying closer to the center of the chart. This tends to produce egg shaped projections of perfectly regular curves on the perimeter surface. The more or less irregular shapes of normal isopters in visual field charts may well be compatible with regular shapes prior to the cartographic deformation. Isopters of different sizes are differently affected.

(II) If the isopter curves on the surface of the perimeter were symmetrical to a point on this surface, they would lose this property during projection and would appear symmetrical only to a meridian. The standard projection thus conceals centers of symmetry, if such exist.

(III) Angular and areal relationships that apply for isopters on the spherical surface are not preserved in the projection. Distances between points on the curves on the sphere are represented proportionally only when they coincide with meridians.

Thus the isopters of the visual field are complexly deformed during their projection to the plane perimetric chart. Several valuable properties from the objective measuring point of view – notably those pertaining to possible conditions of symmetry – are lost in the chart.

There are at least two quite simple ways to minimize or eliminate the cartographic deformation for the purpose of allowing the identification of simple mathematical functions fitting normal isopters (Frisen 1970). Both methods preserve certain properties of symmetry, if such exist. The one method is to change the customary point of fixation during perimetry so as to make the cen-

Fundamentals

The examination of the visual field aims to detect deficiencies in the discriminative ability of a subject within that space where he under steady monocular fixation can perceive light. Deficits of peripheral vision are manifested by contracted spaces and/or impaired perception within subspaces.

The examination usually concerns the photopic differential light sense measured as the ability to distinguish in various directions a light stimulus from a uniformly illuminated background. The very large number of possible variations with respect to physical characteristics of stimulus and background (size shape distance colour etc. cf. Dubois Poulsen 1952) need not be detailed here.

The visual space The space within which a steadily fixating subject can perceive light monocularly is traditionally imagined as a sector of a sphere with its center in the nodal point of the eye. The maximal extent of this conical space is defined by the limits of functional retina. The maximal dimensions may be determined by noting the maximal angular distances relative to the eye and the line of sight at which a strong light stimulus is perceived. The cone may also be characterized by means of a spherical or plane section with the aid of a perimeter and a campimeter (tangent screen) respectively. Such a section which forms a base of the visual space cone defines the visual field.

Vision within the visual space may be characterized by threshold values for perception in selected directions. This is the basis of so called static perimetry. Kinetic perimetry which is the subject of this paper utilizes the fact that the ability to detect a stimulus improves with decreasing angular distances relative to the line of sight. The successive and monotonous change of threshold values allows a meaningful characterization in terms of directions of equal visual efficiency. The kinetic approach involves the use of weaker stimuli than those mentioned above to outline smaller visual cones. A section through such a cone produces a closed curve or *isopter* which represents directions of equal visual efficiency.

An isopter does not normally convey any information as to visual function inside or outside the corresponding visual cone.

Kinetic examinations Kinetic perimetry and kinetic campimetry both utilize a mobile light stimulus which generally is moved from the periphery of the perimetric hemispherical or the campimetric plane towards the central point of fixation. This point is approached from several directions and in each case the subject has to acknowledge when he first perceives the moving stimulus. The point at which the stimulus is perceived is usually determined for eight or twelve equally spaced radii or meridians. The primary data (in terms of spherical or polar coordinates) are transferred to a visual field chart where the points may be joined to approximate the isopter for that particular stimulus. The examination is then repeated with other stimuli so that the visual field finally is characterized by a number of isopters usually two or three which are examined with respect to abnormal features.

Depending on the number of isopters employed there remains larger or smaller parts of the visual space between the nesting cones where visual function escapes representation. In practice isopters do not allow an exhaustive characterization of the visual space. Unrepresented subspaces are usually screened with the aid of a supraliminal stimulus. One procedure consists of a sudden static exposure of a stimulus in unexpected positions within its isopter requesting the subject to acknowledge perceived presentations. An alternative is to continue centripetal stimulus movement beyond the point of initial perception at the same time as the subject is asked to signal its possible disap-

be possible to obtain closely similar isopters from different normal individuals. ■ the normal variability should decrease considerably. Such a procedure would also tend to reduce the variation between examiners. No information is lost by such an approach. It is still possible and actually more simple than previously to compare the sensitivities of different individuals since a subject's sensitivity may be defined in terms of the physical characteristics of his appropriate stimulus for specified points in the visual field.

Except for its lack of flexibility, the main disadvantage of this approach ■ the need of access to sets of finely graduated stimuli. These are not available in the present population of perimeters.

The other approach depends on the widely accepted notion that it is ■ possible to judge isopter shapes subjectively notwithstanding variation in linear dimensions. Obviously this would be impossible if normal isopters did not share characteristics of shape. The nature of such common characteristics is not known but the possibility should be considered that normal isopters, except for random deviations, belong to one and the same family of continuous mathematical functions and differ only with respect to function parameters. It could be that all normal isopters belong to, say, the ellipse family of functions and differ solely as to axis characteristics and midpoint position. If such a family of functions could be approximated by regression methods or if a common feature, say symmetry with respect to a point¹, could be identified, it would be possible to test objectively whether a given isopter, *except for random deviations*, displays normal characteristics or not. The magnitude of function parameters is of secondary interest as emphasized above and with such a character testing approach normal limits no longer would be needed. Another advantage ■ flexibility. This should allow the use of present examination instruments.

Because symmetry with respect to a point is a characteristic of several families of mathematical functions of potential interest, a search for isopter shape characteristics might benefit from an investigation of possible symmetry properties. Symmetry properties of isopters are not so apparent in visual field representations, however, at least not in the case of intermediary and peripheral isopters. This may be due to cartographic distortion consequent to the projection of primary data from the perimeter hemisphere to the plane visual field chart. It is therefore necessary to consider the effects of projection.

Incidentally it may be noted that the chart network in itself seems to induce visual illusion effects interfering with subjective appraisal of isopter shapes (Aren & Frisén unpublished). Possible properties of symmetry may be further obscured during perimetry by prominent facial reliefs and the varying and unsymmetrical covering of the cornea by the eye lids. The latter factor may ex

¹) Symmetry with respect to a point means that the figure in question will coincide with its original position if it is turned less than 360° around the symmetry center.

pearance. Irrespective of procedure a failure to perceive the stimulus denotes impaired vision. Any subspaces of wanting perception are then mapped out by moving the stimulus in various directions from the non seen area and noting the points of renewed perception.

The campimetric technique is used only in studies of the central parts of the visual field

Abnormal findings A localized reduction in visual efficiency appears to be the most important abnormality. Generalized uniform impairments or so called concentric depressions also exist. The latter are generally considered to be non specific. Phenomena of photometric disharmony may also occur (cf. Goldmann 1945, Dubois Poulsen 1966) but seem to be little utilized in clinical work.

The signs of localized defects are somewhat loosely classified as localized isopter depressions and scotomata. The differentiation is partly a matter of procedure partly a matter of topography. Localized isopter depressions are commonly a manifestation of impaired vision within subspaces extending from the central parts of the visual space to its periphery. Because reductions in visual efficiency result in an apparent centripetal displacement of perception thresholds a stimulus presented within a subspace of impaired vision will have to be moved closer than usual towards the point of fixation before perception occurs. Hence the ensuing isopter will show an impression or localized depression corresponding to the directions and the degree of impaired vision. Subspaces of impaired vision which do not engage the limits of the field are termed scotomata. A scotoma often has such a size and shape as to fit between standard isopters. The blind spot corresponding to the optic nerve head is a physiological scotoma.

As a matter of fact the distinctions between scotomata and localized isopter depressions are of limited interest because all scotomata will show up in the form of localized depressions in suitably selected isopters. Actually signs of retinal and visual pathway disturbances may nearly always be thought of in terms of localized isopter depressions. Hence the ability to recognize abnormal isopters will largely determine the yield of the examination.

Methods of isopter characterization Standards of comparison

The results of the examination are obtained in the form of sets of co ordinates for points on isopter curves. The sheer number of observations invites a reduction of the amount of data to be handled in characterizing isopters. Two techniques are sometimes used for this purpose viz the calculation of the average isopter radius and the determination of the area enclosed by an isopter (cf. Ferree Rand & Monroe 1930, 1931, Drance Berry & Hughes 1967).

The average radius of an isopter is obtained simply by adding the angular distances between observed points and the point of fixation and dividing by the number of observations. The resulting value does not convey any information as to the extent of the isopter in various directions. It is thus of little use in diagnostic contexts. This drawback applies also to the determination of the area enclosed by an isopter a technique which suffers from at least two additional disadvantages. Firstly a large number of points must be observed to de-

plain the larger variation in threshold position in the upper part of the field (Fig 9)

The cartographic problem

Even the casual reader of geographical atlases has probably noticed the manifold possibilities of depicting a given geographical region. One and the same global area may assume quite different appearances in different maps. This is due to the fact that there exists no single cartographic projection that is able to represent without faults spherical surfaces in a plane. On the contrary every cartographic projection involves characteristic distortions of linear, angular and/or areal relationships in varying extents across the map. Deformation is an unavoidable consequence of projection. This applies also to the standard cartographic projection of perimetry, the so called polar azimuthal equidistant projection. The deformational properties of this projection have been analysed recently on the basis of a model of the visual space (Frisen 1940). It will suffice to note the following characteristics of deformation here:

(I) Peripheral parts of an isopter outline are depicted on larger scales than parts lying closer to the center of the chart. This tends to produce egg shaped projections of perfectly regular curves on the perimeter surface. The more or less irregular shapes of normal isopters in visual field charts may well be compatible with regular shapes prior to the cartographic deformation. Isopters of different sizes are differently affected.

(II) If the isopter curves on the surface of the perimeter were symmetrical to a point on this surface, they would lose this property during projection and would appear symmetrical only to a meridian. The standard projection thus conceals centers of symmetry, if such exist.

(III) Angular and areal relationships that apply for isopters on the spherical surface are not preserved in the projection. Distances between points on the curves on the sphere are represented proportionally only when they coincide with meridians.

Thus the isopters of the visual field are complexly deformed during their projection to the plane perimetric chart. Several valuable properties from the objective measuring point of view – notably those pertaining to possible conditions of symmetry – are lost in the chart.

There are at least two quite simple ways to minimize or eliminate the cartographic deformation for the purpose of allowing the identification of simple mathematical functions fitting normal isopters (Frisen 1940). Both methods preserve certain properties of symmetry, if such exist. The one method is to change the customary point of fixation during perimetry so as to make the cen-

Fundamentals

The examination of the visual field aims to detect deficiencies in the discriminative ability of a subject within that space where he under steady monocular fixation can perceive light. Deficits of peripheral vision are manifested by contracted spaces and/or impaired perception within subspaces.

The examination usually concerns the photopic differential light sense measured as the ability to distinguish in various directions a light stimulus from a uniformly illuminated background. The very large number of possible variations with respect to physical characteristics of stimulus and background (size shape distance colour etc cf *Dubois Poulsen 1952*) need not be detailed here.

The visual space The space within which a steadily fixating subject can perceive light monocularly is traditionally imagined as a sector of a sphere with its center in the nodal point of the eye. The maximal extent of this conical space is defined by the limits of functional retina. The maximal dimensions may be determined by noting the maximal angular distances relative to the eye and the line of sight at which a strong light stimulus is perceived. The cone may also be characterized by means of a spherical or plane section with the aid of a perimeter and a campimeter (tangent screen) respectively. Such a section which forms a base of the visual space cone defines the visual field.

Vision within the visual space may be characterized by threshold values for perception in selected directions. This is the basis of so called static perimetry. Kinetic perimetry which is the subject of this paper utilizes the fact that the ability to detect a stimulus improves with decreasing angular distances relative to the line of sight. The successive and monotonous change of threshold values allows a meaningful characterization in terms of directions of equal visual efficiency. The kinetic approach involves the use of weaker stimuli than those mentioned above to outline smaller visual cones. A section through such a cone produces a closed curve or *isopter* which represents directions of equal visual efficiency.

An isopter does not normally convey any information as to visual function inside or outside the corresponding visual cone.

Kinetic examinations Kinetic perimetry and kinetic campimetry both utilize a mobile light stimulus which generally is moved from the periphery of the perimetric hemisphere or the campimetric plane towards the central point of fixation. This point is approached from several directions and in each case the subject has to acknowledge when he first perceives the moving stimulus. The point at which the stimulus is perceived is usually determined for eight or twelve equally spaced radii or meridians. The primary data (in terms of spherical or polar co ordinates) are transferred to a visual field chart where the points may be joined to approximate the isopter for that particular stimulus. The examination is then repeated with other stimuli so that the visual field finally is characterized by a number of isopters usually two or three which are examined with respect to abnormal features.

Depending on the number of isopters employed there remains larger or smaller parts of the visual space between the nesting cones where visual function escapes representation. In practice isopters do not allow an exhaustive characterization of the visual space. Unrepresented subspaces are usually screened with the aid of a suprathreshold stimulus. One procedure consists of a sudden static exposure of a stimulus in unexpected positions within its isopter requesting the subject to acknowledge perceived presentations. An alternative is to continue centripetal stimulus movement beyond the point of initial perception at the same time as the subject is asked to signal its possible disap-

ter of symmetry of the isopter under investigation coincide with the perimeter pole, i.e. using parapolar fixation. This will minimize the effects of the varying deformation across the chart and it allows the use of parameters of diametral symmetry. The other method consists of the use of another familiar projection viz the central tangential or gnomonic projection sometimes used in the mapping of central parts of the visual field. This projection can be regarded as a simple extrapolation of the rays defining the visual cones, i.e. it is equivalent to plane rather than spherical sections of the visual cones. It appears unnecessarily complicated to characterize the visual cones by means of their intersections with a spherical surface (as is the case in perimetry) because the configurations of the curves of intersection, i.e. the isopters, will be difficult to grasp and to describe once they deviate from circles. The cones could be characterized directly by means of plane sections for possible ease of analysis. The equivalents of plane sections are easily obtained by central tangential projection of perimetric data. The cartographic deficiencies of this projection (cf *ten Doesschate* 1947) may be ignored in these contexts because the problem is in fact not a cartographical one.

Concluding remarks

The conventional methods of isopter representation certainly introduce difficulties in objective evaluation in that (a) symmetry properties if such exist are concealed. Attempts to describe quantitatively isopter shapes therefore should benefit from changing the customary representation. The alternatives, i.e. the correction of cartographic deformation during analysis or the use of procedures of spherical geometry, would be almost impossible to handle in practice without the aid of computers.

If well fitting mathematical functions or properties of symmetry could be identified and studies of intermediary isopters obtained with parapolar fixation indicate that they appear to display point symmetry (Fig. 3 see also *Frisen* 1970) it would be possible to analyse individual visual field findings objectively with respect to isopter shapes and uniformity of variation. Limits of normal variability would no longer be needed. Space occupying normal records often stored for possible future reference could be replaced with a few notes of relevant characteristics. Rigorously standardized instrumentation would not be needed. Furthermore evaluations of this type might permit the hitherto impossible definition of defect magnitudes in terms of departures from expected values and they might possibly disclose hitherto unknown types of defects. What is perhaps most important is that knowledge of normal isopter shapes appear to be a requisite to the construction of meaningful and sensitive screening proce-

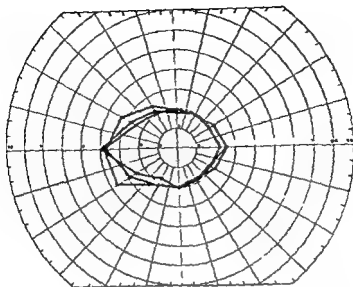


Fig. 1

Observed values for different diameters within an intermediary isopter of a normal emmetropic subject aged 27. Data from three consecutive determinations are superimposed in the chart to illustrate the normal within subject variation under standardized conditions.

A modified Zeiss Jena arc perimeter was used. The instrument was equipped with integral arc illumination ensuring a constant stimulus/background brightness contrast (Frisen 1969) and a synchronous motor mechanism ensuring constant rates of stimulus movement. The rate used here was 2.9/s. On perceiving the stimulus the subject actuated a micro switch interrupting the motor current and applying a braking moment to the rotor. This arrangement prevents the reaction time of the examiner influencing the result. The results were recorded on a built-in punch type chart recorder in the scale 1 mm = 1°. The perimeter also incorporates devices for projecting a fixation target to any desired point within the 20° parallel circle. Here the target was placed in the pole.

The two endpoints of each diameter were determined sequentially, i.e. the arc was not rotated to a new position until both endpoints were determined. The rotation was carried out in such a manner as to preclude learning and fatigue bias.

by a single value (e.g. Ferree *et al.* 1931, Goldmann 1945, Chamlin 1959) of doubtful applicability. On the other hand, knowledge of the limits of normal variation is of little use because the latter are wide enough to accept substantial local depressions. What is needed is a method that in the presence of random variability is able to single out isopters where neighbouring points on the curve show an abnormal relationship to each other, i.e. a method for the detection of aberrations from normal shape. This of course is the guiding principle of the

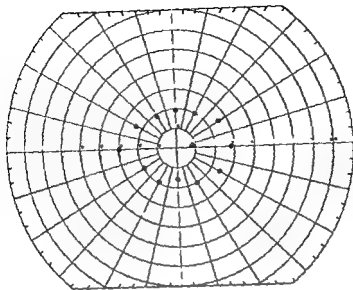


Fig 3

Observed values for different diameters within an intermediary isopter obtained with parapar fixation. The point of fixation (the triangle) was selected so as to make the presumed center of symmetry coincide with the pole. It was tentatively presumed that this point would be situated midway between the point of fixation and the blind spot midpoint (cf Frisen 1960). Except for the changed point of fixation the experimental conditions and the subject were identical with those described in the caption to Fig 1.

These observations and similar data from an additional nine experiments on different normal subjects were subjected to a statistical analysis with respect to departures from point symmetry (diametral symmetry). If an isopter displays point symmetry (except for random deviations) a certain expected value of diameter differences will be independent of the direction of the diameter (cf Frisen 1960). A two way analysis of variance did not disclose any statistically significant departures from symmetry with respect to the selected center.

Such procedures would be of great value because of the time consuming and exacting nature of conventional perimetric examinations (Lynn 1962).

Summary

Previously described methods of visual field isopter characterization are reviewed. These methods give normal limits that are too wide to be of practical value. Furthermore they do not as desired describe the normal relationship between

fine accurately the enclosing curve if only a small number of points are determined and connected by straight lines, as is usually the case the resulting polygon will enclose a smaller area than the real isopter. Secondly the measurement is not valid if it is performed on the standard visual field chart constructed on the principle of equidistant azimuthal polar projection (ten Doesschate 1947 Frisen 1970). This particular type of projection is not cartographically equivalent i.e. the areas enclosed by isopters in the chart are not proportional to the areas enclosed by the isopters on the perimetric hemisphere. Valid determinations of area require the use of other types of charts (ten Doesschate 1947).

There is a large range of normal values for the area enclosed by a standard isopter (i.e. an isopter obtained by a standard stimulus) in the standard chart (Drance et al. 1967) and isopters with subjectively discernible local depressions may well fall within normal limits. This applies also to the average isopter radius which naturally is highly correlated to the enclosed area (Drance et al. 1967).

Because the extent of an isopter in various directions is of crucial diagnostic importance isopters are in practice seldom or never subjected to data reducing handling but remain characterized by the co-ordinates for observed points. Observed data may then be compared with reference data tabulated separately (e.g. Ferree et al. 1931) or inlaid in the visual field chart (e.g. Chamlin 1968). The sources of reference isopters in commercial charts are often unknown. The technique of comparing the two visual fields of one and the same individual requires information as to which one should be considered normal.

The procedure of point to point comparisons between observed data and reference data is mainly applicable to the peripheral part of the visual field where the variation is considerably smaller than in central and intermediary parts (Ferree et al. 1931 Dubois-Poulsen 1966). Unfortunately peripheral isopters are generally considered less valuable from diagnostic points of view than non peripheral ones (Traquair 1939 Blum Gates & James 1959).

There are a large number of variables which influence the dimensions of isopters and cause variation between subjects. Some of these variables also produce variation within subjects i.e. repeated examinations of one and the same subject do not give identical results (Fig. 1).

The result is also influenced by variation within and between examiners. The nature of the sources of variation and possible means of minimizing their influence need not be detailed here (see Lynn 1969). Even under the most carefully standardized conditions of examination there remains a considerable number of uncontrolled or imperfectly controlled sources of variation. These combine to produce normal limits of a remarkable magnitude (Fig. 2).

The distressing degree of normal variability is well reflected by the fact that the standards of comparison seldom or never indicate the extent of permissible variation. The standards are almost exclusively meridian for meridian defined

ter of symmetry of the isopter under investigation coincide with the perimeter pole \Rightarrow using parapolar fixation. This will minimize the effects of the varying deformation across the chart and it allows the use of parameters of diametral symmetry. The other method consists of the use of another familiar projection viz the central tangential or gnomonic projection sometimes used in the mapping of central parts of the visual field. This projection can be regarded as a simple extrapolation of the rays defining the visual cones \Rightarrow it is equivalent to plane rather than spherical sections of the visual cones. It appears unnecessarily complicated to characterize the visual cones by means of their intersections with a spherical surface (as is the case in perimetry) because the configurations of the curves of intersection \Rightarrow the isopters will be difficult to grasp and to describe once they deviate from circles. The cones could be characterized directly by means of plane sections for possible ease of analysis. The equivalents of plane sections are easily obtained by central tangential projection of perimetric data. The cartographic deficiencies of this projection (cf *ten Doesschate* 1947) may be ignored in these contexts because the problem is in fact not \Rightarrow cartographical one.

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The conventional methods of isopter representation certainly introduce difficulties in objective evaluation in that \Rightarrow a symmetry properties if such exist are concealed. Attempts to describe quantitatively isopter shapes therefore should benefit from changing the customary representation. The alternatives \Rightarrow the correction of cartographic deformation during analysis or the use of procedures of spherical geometry would be almost impossible to handle in practice without the aid of computers.

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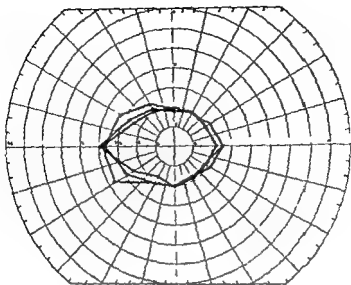


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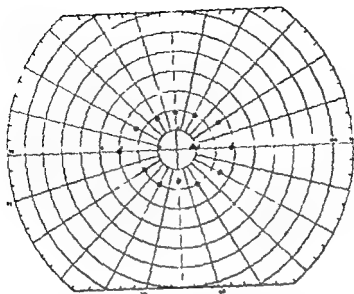


Fig. 3

Observed values for different diameters within an intermediary isopter obtained with parapolar fixation. The point of fixation (the triangle) was selected so as to make the presumed center of symmetry coincide with the pole. It was tentatively presumed that this point would be situated midway between the point of fixation and the blind spot midpoint (cf. *Fruen 1960*). Except for the changed point of fixation the experimental conditions and the subject were identical with those described in the caption to Fig. 1.

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Such procedures would be of great value because of the time consuming and exacting nature of conventional perimetric examinations (*Lynn 1962*).

Summary

Previously described methods of visual field isopter characterization are reviewed. These methods give normal limits that are too wide to be of practical value. Furthermore, they do not, as desired, describe the normal relationship between

years (table IV) A similar observation period for the total series gave only an average of 1.4 attacks (table III)

Thus the IDU treated had a greater number of relapses

Recurrence after Steroid Therapy

Steroid therapy was mainly employed in cases of corneal oedema and impending metaherpetic development

Recurrence seemed to be more frequent after steroid treatment than after no treatment (table IV) This difference may however be accountable for by longer observation of the steroid treated The increased number of relapses corresponds in fact approximately to the longer observation period (cf table III)

In other words the steroid treatment has not been shown to cause any significant alteration of the recurrence rate

Table IV

Number of attacks considered in relation to therapy (IDU steroid iodine cauterisation)
109 patients with herpetic keratitis

therapy	1	2	3	4	5	>5	aver number of attacks	obs period	number of patients
IDU	18	16	6	4	3	7	4.0	12.2	56
no IDU	25	10	10	1	2	5	2.7	13.8	53
IDU	27	18	3	0	2	4	9.5	5.6	56
steroid	1	10	2	4	11	3	4.7	14	38
no steroid	31	16	14	1	5	4	9.6	10.4	71
cauterisation	7	19	15	4	6	11	3.9	14.4	82
no cauterisation	16	7	1	1	1	1	1.9	8.5	27
steroid and/or IDU	25	19	7	4	11	12	4.1	12.5	73
neither steroid nor IDU	14	7	9	1	1	11	1.9	13.8	36
metaherpetic	15	1	5	3	4	9	4.1	13.9	33
not metaherp	4	9	11	2	3	3	9.7	10.0	56
Total	44	6	16	5	7	12	3.4	13.0	109

1 = time from the point of time at which the first IDU treatment was instituted

disadvantage that 17 per cent of the patients had died at the time of the follow up and therefore had to be ruled out

The number of relapses was seen to depend largely on the time of the follow up as shown in table III With an observation time of 5.6 years the average number of attacks was no more than 1.4 (0.4 relapses) An observation period of 18 years, on the other hand disclosed on an average 7 attacks (6 relapses) Observation of more than 2 attacks in the same patients required an observation period exceeding 11 years

After an observation period of more than 18 years only one recurrence free case was seen (a man aged 68 observed for 35 years)

The conclusion may be drawn that a very long observation period is required before it is possible to pronounce approximately on the recurrence rate The figures show that the chance of recurrence is great provided the observation period is sufficiently long Recurrence may be experienced after a recurrence free interval of many years

Recurrence after IDU Therapy

The number of attacks among patients treated with IDU was greater (average 4.0) than among those never given IDU

IDU therapy was introduced later than the other treatments The mean observation period was therefore shorter for the IDU treated The proper increase of relapses after IDU must therefore be higher than the figures suggest

By including solely the period after the first IDU treatment had been prescribed on an average 2.5 attacks were found after an observation period of 2.6

Table III

Number of attacks considered in relation to length of observation period 109 patients with herpetic keratitis

Obs period in years	aver number of attacks	number of patients
---------------------	------------------------	--------------------

5-6	1.4	23
7-8	1.9	15
9-10	2.2	25
11-12	3.6	17

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VARIA

International Society of Geographical Ophthalmology

Following the First International Congress on Regional Ophthalmology held in Yellowknife, N W T Canada, in June 1970 an *International Society of Geographical Ophthalmology* was formed.

The co-opted executive committee formed was composed of 1 Professor Ida Mann Nedlands West Australia 2 Professor M E Weigelin, Institute of Experimental Ophthalmology Bonn, Germany 3 Dr Alberto Lancia Buenos Aires Argentina 4 Dr Abraham Hornzweig New York City U S A 5 Dr Wm John Holmes Honolulu Hawaii Secretary ■ Dr E Cass Northwest Territories Canada President

It is proposed to have two research centers one in Yellowknife N W T Canada and one in Bangkok As much information as possible will be collected on all work already done on Geographical Ophthalmology in order to ascertain the total factors causing ophthalmic conditions and their distribution throughout the world It is hoped it will be possible to find out the areas where research is inadequate or non-existent and to encourage research where necessary

It is proposed that the next meeting be held in two years time either in Israel or in Auckland A bulletin shall be published from time to time giving papers on research in Geographical Ophthalmology

The yearly subscription shall be ten dollars per annum to get the society incorporated and send to Mr Mark de Weerd Q C I O Box 939 Yellowknife N W T Canada

10.-13 Juni 1971 Jahreshauptversammlung der Österreichischen Ophthalmologischen Gesellschaft in Linz

Anfragen und Anmeldungen sind an Doz Dr W Funder erbeten Wiener Medizinische Akademie für ärztliche Fortbildung, Spitalgasse 9 1 1090 Wien IX Österreich Sprechzeit Vorträge 10 Minuten Mitteilungen und Demonstrationen ■ Minuten Anmeldeschluss für wissenschaftliche Beiträge 1. Mai 1971

Course in Retinal Detachment

The Retina Service Massachusetts Eye and Ear Infirmary will sponsor the 9th Annual course in Retinal Detachment on May 20 21 and 22 1971 The curriculum will include lectures covering the fundamentals of fundus diagnosis pathogenesis and modern methods of treatment of detached retinas Tuition is \$125 for practitioners Residents \$50 upon application from Department Head Checks are payable to Massachusetts Eye and Ear Infirmary and should be sent to Ronald C Pruett M D Retina Service Massachusetts Eye and Ear Infirmary 743 Charles Street Boston Massachusetts 02114

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neighbouring points on isopter curves Possible approaches to the quantitative definition of the shapes of normal isopters amidst random variability are discussed and illustrated

References

- Blum F G Gates L K & James B R How important are peripheral fields? *Arch Ophthal* 61 1-8 1959
- Chamlin M An isopter in the intermediate field of vision *Arch Ophthal* 61 608-615 1959
- Chamlin M Methodology and techniques in visual field studies *Survey Ophthal* 15 91-117 1968
- Doesschate J ten Perimetric charts in equivalent projection allowing a planimetric determination of the extension of the visual field *Ophthalmologica* 113 251-260 1947
- Drance S M Berry V & Hughes A Studies in the reproducibility of visual fields areas in normal and glaucomatous subjects *Canad J Ophthal* 1 14 1966
- Drance S M Berry V & Hughes A Studies on the effects of age on the central and peripheral isopters of the visual field in normal subjects *Amer J Ophthal* 63 1667-1762 1967
- Dubois Poulsen A Le champ visuel Topographie normale et pathologique de ses sensibilités Paris Masson et Cie 1952
- Dubois Poulsen A Etude critique des techniques d'examen de la vision périphérique *Canad J Ophthal* 1 24-35 1966
- Ferre C E Rand G & Monroe M M Studies in perimetry 4 Preliminary work on a diagnostic scale for the form field with a 0.17 degree stimulus *Amer J Ophthal* 13 859-867 1930
- Ferre C E Rand G & Monroe M M Diagnostic scales for the 1 degree and 0.17 degree form field stimuli for the eight principal meridional quadrants taken separately *Arch Ophthal* 6 518-534 1931
- Fisher R F The variations of the peripheral visual fields with age *Docum ophthal* 24 41-61 1968
- Frisen L Integral arc illumination for projection perimeters *Acta ophthal* 47 1176-1180 1969
- Frisen L The cartographic deformations of the visual field *Ophthalmologica* 161 38-54 1970
- Frisen M Regressionsproblem inom synfeltsforskning MA thesis Department of Statistics University of Göteborg
- Goldmann H Grundlagen exakter Perimetrie *Ophthalmologica* 109 51-10 1945
- Harrington D O The visual fields A textbook and atlas of clinical perimetry 2nd ed Saint Louis C V Mosby Co 1964
- Lloyd J P F Making perimetry pay *Trans ophthal Soc UK* 11 409-418 1947
- Lynn J R Current trends in quantitative perimetry *Int Ophthal Clin* 9 49-75 1967
- Lynn J R Examination of the visual field in glaucoma *Invest Ophthal* 8 16-24 1969
- Traquair H M Clinical detection of early changes in the visual field *Arch Ophthal* 22 941-967 1939

Aberg L vide *Bynke H G*

Assied H Osteopetrosis from the ophthalmological point of view A report of two cases

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years (table IV). A similar observation period for the total series gave only an average of 1.4 attacks (table III).

Thus the IDU treated had a greater number of relapses.

Recurrence after Steroid Therapy

Steroid therapy was mainly employed in cases of corneal oedema and impending metaherpetic development.

Recurrence seemed to be more frequent after steroid treatment than after no treatment (table IV). This difference may, however, be accountable for by longer observation of the steroid treated. The increased number of relapses corresponds in fact approximately to the longer observation period (cf. table III).

In other words, the steroid treatment has not been shown to cause any significant alteration of the recurrence rate.

Table IV
Number of attacks considered in relation to therapy (IDU, steroid, iodine cauterisation)
109 patients with herpetic keratitis

therapy	1	2	3	4	5	>5	aver number of attacks	obs. period	number of patients
IDU	18	16	6	4	5	7	4.0	19.2	56
no IDU	25	10	10	1	2	5	2.7	13.8	53
IDU	27	18	3	2	0	4	9.5	5.6	56
steroid	17	10	2	4	0	3	4.7	14	58
no steroid	31	16	14	1	5	4	9.6	12.4	71
cauterisation		19	15	4	6	11	3.9	14.4	82
no cauterisation	16	7	1	1	1	1	1.9	8.5	27
steroid and/or IDU	5	19	7	4	6	19	4.1	19.5	73
neither steroid nor IDU	15	7	9	1	1	0	1.9	13.9	56
metaherpetic not metaherp.	15	17	5	3	4	9	4.1	13.9	53
	9	9	11		3	3	9.7	12.0	56
Total	49	67	16	5		12	3.4	15.0	109

reckoned from the point of time at which the first IDU treatment was instituted.

Recurrence after Iodine Cauterisation

Local iodine cauterisation on the dendritic process is the earliest one of the treatments instituted. The mean observation period was therefore longer for the patients thus treated than for the others.

The longer observation period can fully explain the apparently increased recurrence rate. The recurrence rate could not be demonstrated to have altered under the influence of cauterisation.

Some of the cauterized patients had been treated with IDU and/or steroid (table V). Unfortunately it was impossible to tabulate groups subjected to any one pure treatment because the number of cases within each of such groups would be too small in the series under review.

The patients given neither IDU nor steroid had fewer relapses. The recurrence rate seemed to be unaltered after iodine cauterisation.

Recurrence after Metaherpetic Development

In 53 of the 109 patients the lesion penetrated into deeper layers at some time or other, having therefore been characterized as metaherpetic in the case record.

The mean observation period was a little longer for the metaherpetic cases. The recurrence rate seemed not to be significantly raised among these compared with the more superficial cases (table IV).

Visual Impairment

Two of the 109 patients with herpetic keratitis were subjected to corneal transplanation. The degree of visual impairment therefore could not be estimated in these two cases.

Table V

Treatment of 109 patients with herpetic keratitis. The figures represent the percentage numbers of patients given the combined treatment concerned (56 IDU treated, 38 steroid treated and 82 cauterized).

	also subjected to		
	IDU	Steroid	Cauterisation
treated with IDU	—	98	54
treated with steroid	55	—	19
treated by cauterisation	37	31	—

Table 11
Visual acuity at follow up of 107 patients after lepidontic keratitis (Best vision stated in 11 bilateral cases)

	< 6/60	< 6/36	< 6/24	< 6/18	< 6/12	< 6/9	< 6/6	no of pts
IDU	3	11		1	3	11	11	34
in IDU	3	1	3	3	7	6	9	39
steroid	4	9	11	1	6	7	6	36
no steroid	9	1	9	3	3	10	13	71
cauterisation	4	9	3	3	9	13	15	91
no cauterisation	9	1	0	1	1	4	4	26
steroid or IDU	5	3	3	2	7	19	13	71
neither steroid or IDU	1	0	9	9	9	5	6	36
metaherpetic	6	9	4	1	7	8	10	51
not metaherpetic	0	0	1	3	2	9	9	50
Total	6	3	5	4	9	17	19	107

In the 11 bilateral cases only the eye with the least visual impairment i.e. the eye used by the patients in practice was tabulated

The visual acuity recorded is that obtained with the best possible correction but without use of stenopæic hole or split

In eight cases the visual impairment was due not only to corneal opacity after previous herpetic keratitis but also to senile central retinal degeneration or cataract. In these cases the visual impairment due to the corneal defect alone was roughly estimated. The visual acuity recorded was therefore better than that measured at the follow up

Astigmatism was frequent especially among patients with diffuse corneal opacity and considerable visual impairment (35 of the 107 patients had astigmatism ≥ 1 dioptre 18 ≥ 2 dioptries and 5 ≥ 4 dioptries)

The visual acuities at the follow up are shown in table VI. All the patients are supposed to have had a normal vision (6/6) before the first attack of herpetic keratitis

Only six out of 107 had under 6/60 at the follow up

Visual Impairment after IDU Therapy

At the follow up there was no difference in visual acuity between the IDU treated and those given no IDU (table VI) in spite of the fact that recurrences were more frequent among the former

Accordingly we may conclude that the individual attacks are less harmful to the patient's vision when IDU is given but that the changes of fresh relapses are greater. The final visual impairment is of the same order for IDU treated and untreated

Visual Impairment after Steroid Therapy

The steroid treated had a poorer vision than the non steroid treated. This may be due to the fact that steroid was preferably given to patients whose disease had reached a bad phase being under metaherpetic development with visual impairment before the treatment was started. We therefore cannot draw definite conclusions concerning the effect of steroids on the vision

The patients given neither IDU nor steroid experienced the least visual impairment

Visual Impairment after Iodine Cauterisation

In 81 iodine cauterized patients the final degree of visual impairment was approximately the same as in 26 non cauterized. Cauterisation is probably mainly performed in the fairly grave cases and the cauterisation itself may tend to

augment cicatrization if deep. One aims however at not penetrating below the level of Bowman's membrane. Cauterization could not be demonstrated to have any deleterious effect on the visual acuity. On the contrary if the cauterized cases may be regarded as particularly grave the cauterization had a vision preserving effect if anything.

Visual Impairment after Metaherpetic Development

As might be expected the mean visual impairment was much greater after metaherpetic development than in the cases where the herpetic keratitis remained superficial (table VI).

DISCUSSION

In the present study it was aimed at obtaining an observation period sufficiently long to give an impression of the true recurrence rate. The mean observation period was 13 years. The affection recurred in 61 per cent of the cases with on an average 3.4 attacks per patient in the total series.

The observation periods are shorter or unknown in previously published studies and the recurrence rates found are considerably lower than in the present series.

Davidson noticed recurrence in 16 per cent (51 patients). Caperrucci in 15 per cent (obs. 6-7 months IDU treated). Carroll *et al* in 26 per cent not previously affected with dendritic keratitis and in 43 per cent with previous attack (2 years of observation, 159 patients).

Cilker found recurrence in 40 per cent (159 patients). Kaufman (1963) and Gordon in one third of IDU treated. Patterson in 10 per cent (84 patients obs. 13 months). Sood in 11 per cent (150 patients obs. period unknown). Laibson 11 per cent (100 patients obs. less than 1 year). Thygesson 40 per cent (200 patients). Thomas *et al* 15 per cent (119 patients).

Cundersen found on an average 2.1 attacks per patient (221 patients, retrospective investigation and further 3 1/2 years of observation, the mean obs. period unknown).

The higher recurrence rate in the series under review is probably mainly due to the longer observation period as it could be shown that the observation period has an influence on the recurrence rate found and that relapses may occur very long after the first attack.

However geographic, seasonal and therapeutic factors may also influence the recurrence rate (Laibson).

In the present study IDU treatment was seen to involve an increased risk of recurrence.

Patterson saw recurrence in seven out of 43 IDU treated against in only one

In the 11 bilateral cases only the eye with the least visual impairment i.e. the eye used by the patients in practice was tabulated

The visual acuity recorded is that obtained with the best possible correction but without use of stenopæic hole or split

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In 81 iodine cauterized patients the final degree of visual impairment was approximately the same as in 26 non cauterized. Cauterisation is probably mainly performed in the fairly grave cases and the cauterisation itself may tend to

tabolites will appear whose properties are superior to those of IDU preferably such as to reduce the chance of recurrence

The degree of visual impairment after dendritic keratitis constitutes a practical measure of the functional damages caused by the disease. In the present study it has therefore been employed as a measure of the effect or failing effect of the therapy. However the visual impairment also depends on the site of the keratitis (most pronounced at central localisation)

It will therefore be appropriate to report other parameters from the follow up. This will be done in some future papers (corneal opacity, vascularisation, Fischer-Schweitzer's fluorescam pattern, permanent holes in the precorneal film, vital staining and corneal sensitivity)

Summary

The above study was based on a series of patients with dendritic (herpetic) keratitis referred within a seven year period to an ophthalmic out-patient department. The series comprised 157 patients of whom 109 were followed up.

The incidence was calculated at 1/196 among all ophthalmic patients with a male preponderance (59 per cent males). The age distribution at first attack showed that the majority were children or patients between the ages of 40 and 50. 10 per cent were bilateral and 6 per cent probably primary. No seasonal variations were detected.

Relapses were frequent (in 61 per cent) with an average of 3.4 attacks per patient. The interval between the first and the second attack averaged 5.7 years and that between the first and the latest one recorded 13.4 years (mean observation period 13 years).

The recurrence rate was higher for the IDU treated than for the non IDU treated but the recurrences seemed to run milder courses, the final visual impairment being of the same degree in the two groups.

Steroid therapy apparently caused graver visual impairment.

Iodine cauterisation seemed to have no influence on the recurrence rate nor add to the visual impairment.

Acknowledgement

The above study was aided by a grant from *Cykelhandler P. Th. Pasmussen og hustru Nina Pasmussen's Mindelegat*.

Mrs S. Meulitz, a secretarial under-taker, undertook inquiries at National registration offices and arranged the summoning of patients for the follow up.

out of 41 placebo treated *Davidson Burns* and *Hughes* suggested the possibility of earlier recurrence after IDU while *Carroll et al* found no difference

Previous investigations have been concentrated particularly on the question whether IDU can shorten the active phase of herpetic keratitis

If a shortened period of treatment implies less pain less cicatrization of the cornea less visual impairment and a reduced chance of recurrence the treatment is ideal

However the present investigation gave results suggesting that IDU adds to the chance of recurrence On the other hand the treatment did not entail a poorer visual prognosis Thus the numerous fairly short relapses seemed not to be more dangerous than the spontaneous course with fewer but more protracted attacks

The different forms of therapy are difficult to compare because they may be given at different indications dependent on the severity of the affection

IDU has however been given as a routine since the introduction of the drug

A steroid has often been given in particularly difficult cases The apparently poor final visual response to this treatment is therefore difficult to assess

The series under review presented no cases of iatrogenic chronic dendritic kerato uveitis in *Thygeson's* sense nor fatal cases with secondary bacterial or mycotic infection

Cauterisation with iodine seemed not to increase the risk of recurrence or the visual impairment

Several patients of the present series were treated with two or more drugs If series subjected to only one therapy each were available the differences would probably stand out more clearly The IDU treated groups would then presumably show a greater number of relapses and the steroid treated a more pronounced visual impairment

A rational therapy against dendritic keratitis is difficult to suggest on the basis of the results achieved from the present investigation

IDU treatment must be warned against owing to the increased chance of recurrence possibly due to the cytotoxic effect of the drug IDU should perhaps be given for a short period only

The risk involved by steroid treatment has been suggested in this paper and borne out by *Thygeson* among others

The conventional cauterisation seems not to add to the risk of recurrence or visual impairment

In agreement with *Davidson* we may recommend treatment of dendritic keratitis with IDU for one week If this treatment does not cure the affection completely the remaining active area should be subjected to iodine cauterisation The IDU treatment has a definitely rational basis It is however no ideal therapy

It is to be hoped – and may probably be expected – that other virus antime

- Lambson Peter R & Irving Leopold* An evaluation of double blind IDU therapy in 100 cases of herpetic keratitis *Trans Am Acad. Ophthal Otolaryng* 68 22 34 (1964)
- Macken M A D* A comparison of IDU solution IDU ointment and carbolic acid in the treatment of dendritic corneal ulcer *Brit. J Ophthal* 48 274 2 6 (1964)
- Mach H & Z Wilek* Über die Behandlung der Keratitis herpetica mit IDU *Klin Monatsbl Augenheilk* 146 270 274 (1965)
- Maxwell Earl* Treatment of herpes keratitis with 5 iodo 2 deoxyuridine (IDU) A clinical evaluation of 1500 cases *Am J Ophthal* 56 571 573 (1963)
- Nataf Roger Pierre Lépine & Georges Bonamour* *Oeil et virus* pp 1022 Masson et C Paris (1950)
- Patterson Alan Antony D Fox Geoffrey Davies Charles Maguire P J Holmes Sellers Peter Wright N S Rice Benjamin Cobb & Barrie P Jones* Controlled studies of IDU in the treatment of herpetic keratitis *Trans Ophthal Soc U K* 83 583 591 (1963)
- Sood N N & V J Morrison* Superficial herpetic keratitis treated with 5 iodo 2 deoxyuridine *Brit J Ophthal* 48 609 614 (1964)
- Thomas Charles I Edward W Purnell & Melvin S Rosenthal* Treatment of herpetic keratitis with IDU and corticosteroids Report of 10 cases *Am J Ophthal* 60 204 217 (1965)
- Thygeson P S J Kimura & M J Hogan* Observations on herpetic keratitis and keratoconjunctivitis *Arch Ophthal* 56 375 383 (1956)
- Thygeson Ph & Samuel J Kimura* Deep forms of herpetic keratitis *Am J Ophthal* 43 part II 109 113 (1957)
- Thygeson Phillips* Chronic herpetic keratouveitis *Trans Am Ophthal Soc* 65 211 216 (1967)

References

- Anseth Arvid & Kjeld Dyster Aas* Herpes simplex keratitis treated with 5 iodo 9 deoxyuridine *Acta Ophthal* 42 345 346 (1964)
- Brandt H P & H Zenker* Die Bedeutung des Wetters für die Auslösung des Herpes corneae *Klin Monatsbl Augenheilk* 145 518 525 (1964)
- Burns Robert P* A double blind study of IDU in human herpes simplex keratitis *Arch Ophthal* 70 381 384 (1963)
- Burns Robert P* discussion Laibson *Trans Am Acad Ophthal Otolaryng* 68 34 (1964)
- Capperucci G* Clinical observations of IDU in the treatment of herpes corneae *Ann Ottal* 91 1312 1322 (1965)
- Carroll John M Eeva Lusa Martola Peter R Laibson & Claes H Dohlman* The recurrence of herpetic keratitis following Idoxyuridine therapy *Am J Ophthal* 60 103 107 (1964)
- Davidson S I & J Jameson Evans* IDU and the treatment of herpes simplex keratitis *Brit J Ophthal* 48 648 653 (1964)
- Dawson Chandler Brigitta Togni & Thomas E Moore* Structural changes in chronic herpetic keratitis *Arch Ophthal* 79 740 747 (1963)
- Ej R C & W F Hughes A W Holmes & F Deinhardt* Clinical and laboratory evaluations of idoxyuridine (IDU) therapy in herpes simplex keratitis *Arch Ophthal* 71 325 331 (1964)
- Gilkes M J* Further experiences in the therapy of herpetic and other keratitis with 5 iodo deoxyuridine (IDU) in hospital practice *Trans Ophthal Soc UK* 83 593 601 (1963)
- Gordon Dan M & David A Karnofsky* Chemotherapy of herpes simplex keratitis *Am J Ophthal* 55 229 234 (1963)
- Grut Edm Hansen* Two typical forms of keratitis *Congres international des Sciences medicales 8 session Copenhagen 1884 Tom 3* 34 40 (1886)
- Gundersen Trygve* Herpes corneae With special reference to its treatment with strong solutions of iodine *Arch Ophthal* 15 225 249 (1936)
- Hart D R L & J F Brightman G G Readshaw G T J Porter & M J Tulby* *Arch Ophthal* 73 623 634 (1965)
- Hughes William F* Treatment of herpes simplex keratitis *Am J Ophthal* 67 313 328 (1969)
- Jepson C N* Treatment of herpes simplex of the cornea with IDU - A double blind study *Am J Ophthal* 57 213 217 (1964)
- Jones Barric R B F Andrews W G Henderson & P Schofield* Pattern of conjunctivitis at Moorfields during 1956 *Trans Ophthal Soc UK* 47 291 305 (1957)
- Jonkers G H* Statistical investigations on the occurrence of herpes simplex corneae *Ophthalmologica* 144 405 408 (1962)
- Kaufman H E A B Nesburn & E D Maloney* *Arch Ophthal* 67 583 591 (1962)
- Kaufman H E E L Martola & C Dohlman* Use of 5 iodo 2 deoxyuridine (IDU) in the treatment of herpes simplex keratitis *Arch Ophthal* 68 235 239 (1962)
- Kaufman H E E L Martola & C H Dohlman* Herpes simplex treatment with IDU and corticosteroids *Trans Am Acad Ophthal Otolaryng* 64 695 701 (1963)
- Kaufman Herbert E* Epithelial erosion syndrome metaherpetic keratitis *Am J Ophthal* 57 953 957 (1964)
- Kaufman H E D C Brown & E D Ellison* Herpes virus in the lacrimal gland conjunctiva and cornea of man - a chronic infection *Am J Ophthal* 65 32 35 (1968)

- Labson Peter R & Irving Leopold* An evaluation of double blind IDU therapy in 100 cases of herpetic keratitis *Trans Am Acad Ophthal Otolaryng* 68 27 34 (1964)
- Mackenzie A D* A comparison of IDU solution IDU ointment and carbolicization in the treatment of dendritic corneal ulcer *Brit J Ophthal* 48 274 276 (1964)
- Mach H & Z Walek* Über die Behandlung der Keratitis herpetica mit IDU *Klin Monatsbl Augenheilk* 146 270 274 (1965)
- Maruelli Earl* Treatment of herpes keratitis with 5 iodo 2 deoxyuridine (IDU) A clinical evaluation of 1500 cases *Am J Ophthal* 56 571 573 (1963)
- Nataf Roger Pierre Lepine & Georges Bonamour* *Oeil et virus* pp 102 Masson et C Paris (1960)
- Patterson Alan Antony D Fox Geoffrey Davies Charles Maurice P J Holmes Sellers Peter Wright N E Rice Benjamin Cobb E Barrie R Jones* Controlled studies of IDU in the treatment of herpetic keratitis *Trans Ophthal Soc U K* 89 583 591 (1963)
- Sood N V & V J Morrison* Superficial herpetic keratitis treated with 5 iodo 2 deoxyuridine *Brit J Ophthal* 48 609 614 (1964)
- Thomas Charles I Edward W Purnell & Melvin S Rosenthal* Treatment of herpetic keratitis with IDU and corticosteroids Report of 105 cases *Am J Ophthal* 60 904 917 (1965)
- Thygeson P S J Kimura & M J Hogan* Observations on herpetic keratitis and keratoconjunctivitis *Arch Ophthal* 6 375 378 (1956)
- Thygeson Ph & Samuel J Kimura* Deep forms of herpetic keratitis *Am J Ophthal* 43 part II 109 113 (1957)
- Thygeson Phillips* Chronic herpetic keratouveitis *Trans Am Ophthal Soc* 65 211 226 (1967)

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MICROPUNCTATE FLUORESCEIN VITAL STAINING OF THE CORNEA

BY

M S NORN

Vital staining of the cornea with fluorescein is employed for controlling among other things the state of the cornea of contact lens wearers the fluorescent areas being assessed in cobalt filtered light in the slit lamp

Fluorescein only penetrates into the corneal epithelium at the sites of interrupted continuity of the epithelial surface The dye thus discloses lesions of the corneal epithelium

A peripherally localized fluorescein stained corneal area may be due to the contact lens being too curved with the result that the edge of the lens or its intermediary curve injures the cornea

If, on the other hand the stained area is found centrally the lens may be too flat thus directly eroding the central corneal zone or it may on the contrary be so greatly curved as to cause deficient ventilation of tear fluid and consequently a tendency to central oedema of the cornea In the stated cases the lens should be modified

In some instances a diffuse fluorescein staining is seen in the form of numerous minute dots This phenomenon is not infrequently observed during the adaptation period and is possibly accountable for by a too liberal adaptation schedule

In some eyes we see only very few minute fluorescein dots on the cornea In principle such dots must be regarded as minor lesions of the corneal epithelium

These may equally well as larger erosions become the point of entrance of bacteria fungi and virus

The more closely the cornea is inspected for fluorescein staining the more often such is found. The question is whether fine punctate fluorescein staining may be a physiological phenomenon and whether a certain minimum fluorescein staining ought to be tolerated in practice as inevitable also in contact lens wearers

In an previous study (Norn 1964 A) I showed that punctate fluorescein staining may be seen in normals on the palpebral conjunctiva (in 21 per cent) and on the caruncle in the latter area presumably only in the hair follicles

No proper fluorescein staining was detectable on the cornea of normals or of patients with corneal degeneration or conjunctivitis

Using a special careful technique of examination it is however possible to detect small fluorescein stained dots even in normal eyes. In the present paper the phenomenon is termed micropunctate fluorescein staining

Method

As vital stain is used fluorescein at a concentration of 0.125% or 1% the latter concentration in combination with 2% rose bengal to be able to compare the results of these two vital stains differing in principle

One of the following three dye solutions is used

- 1) 0.125% fluorescein rendered isotonic with NaCl with no preservative added
- 2) A fluorescein oxibuprocaine mixture acc. to Fenton containing 0.125% fluorescein 0.3% oxibuprocaine chloridum (NF¹⁴) (novesin Wander an anaesthetic) and 0.001% phenylmercuric nitrate as preservative and NaCl for isotonia
- 3) A fluorescein rose bengal mixture 50 mg fluorescein, 50 mg rose bengal 40 mg NaCl and distilled water to 5 g with 0.001% phenylmercuric nitrate added

The pH values of these dye solutions range from 6.37 to 7.70

The dye solution is instilled into the inferior conjunctival fornix from a needle mounted tube yielding a drop of 0.01 ml (Norn 1964 B)

The patient blinks a few times after which the cornea is observed in cobalt filtered light in the slit lamp. The examination is repeated after 1-2 minutes to record the finest punctate staining which may have been concealed by staining of the precorneal film on the first examination

Examination is repeated until the colour of the precorneal film is so pale that it can no longer be suspected to interfere with a possible staining of the corneal epithelium

The minute fluorescein stained dots are counted and the number entered in a table

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Table I

Age distribution of normals presenting micropunctate fluorescein staining

Age	fluorescein 0.125%		fluorescein 1% and rose bengal 1%	
	% stained	number exam	% stained	number exam
< 40	4	40	0	10
40-49	13	60	67	6
50-59	20	106	82	22
60-69	19	117	83	6
≥ 70	20	81	40	0
Total	17	411	73	49

Table II

Micropunctate fluorescein staining of normal eyes Sex distribution and dependence on dye solution The figures indicate the percentage numbers of subjects whose eyes were stained

	women	men	Total	number of eyes examined
0.125% oxibuprocaine fluorescein	16	17	16	340
0.125% fluorescein	04	18	01	11
1% rose bengal combined with 1% fluorescein	81	60	73	49
Total	93	23	23	460

fluorescein combined with 1% rose bengal as many as 30 per cent of this group had more than 1000 dots scattered over the cornea (table III)

The minute dots rose in number with increasing years. The subjects under 40 presented maximally 9 dots while up to 100 dots or more could be seen after the age of 60 after instillation of 0.125% fluorescein (fig. 1)

A similar rise was seen after instillation of a mixture of 1% rose bengal fluorescein with maximum 9 dots before the age of 30 against up to 100 000 diffusely over the cornea after the age of 50

Material

The total material examined comprised 460 normal eyes and 192 pathological from 326 subjects. The diagnoses in the pathological cases are shown in table IV.

Results

Micropunctate fluorescein staining was most frequently seen after instillation of 1 % fluorescein combined with 1 % rose bengal.

There seemed on the other hand to be no difference between the eyes treated with 0.125 % fluorescein alone and those also given oxibuprocaine (Novesin) and a preservative. The two latter groups have therefore been dealt with collectively in the paper.

Normals

Incidence of Micropunctate Staining

One normal out of every six showed micropunctate staining of the cornea after instillation of 0.125 % fluorescein. The number having stainable corneae was seen to rise with increasing years. Micropunctate staining was observed in no more than 4 % of normals under 40 years of age against in 20 per cent over 50. The incidence seemed to rise steadily until the age of 50 and then to remain unchanged.

Micropunctate fluorescein staining was even more frequent after instillation of 1 % fluorescein combined with 1 % rose bengal. This gave staining in 73 per cent of the normals examined. The frequency of stained corneae followed approximately the same age curve as that after the weaker fluorescein (table I).

No unquestionable sex difference was detectable. The possible female preponderance after staining with rose bengal and fluorescein (table II) was not statistically significant. The larger fluorescein oxibuprocaine stained series showed no sex difference.

Number of Minute Dots

After instillation of 0.125 % fluorescein minute dots were seen in 17 per cent of the normals. In most cases the number of such dots was very small and only recognizable by the technique described above. No more than 1 per cent displayed over 100 dots (table III).

The number of dots seen was considerably greater after instillation of 1 %

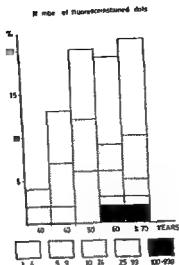


Fig 1

Micropunctate fluorescein staining of normal corneae Dependence on age
 411 eyes stained with 1% fluorescein Abscissa patient's age Ordinate Percentage
 number of eyes stained The hatching and colouring of the columns indicate the number
 of minute dots per cornea

In the presence of many dots the counting was based on an estimate. The dots within a corneal area exposed to light through a suitably small slit were counted. The total number was thereafter calculated from this value. Maximum was 10^3 in normal cases and perhaps 10^4 in pathological. In the latter the cornea was spotted with almost confluent fine dots.

Pathological Cases

This report does not include true fluorescein staining where a fairly large area is distinctly stained as seen for instance in cases of erosion. Fluorescein staining could be expected in only few cases of the present series (table IV).

Nevertheless micropunctate fluorescein staining was more frequent and more extensive than in normals.

Such staining with roughly up to 10^4 minute dots was frequent in cases of conjunctivitis sicca, corrosion and foreign bodies on the cornea and also relatively frequent in keratitis, corneal dystrophy and corneal opacity.

Minute dots were also more frequent in the presence of such diseases as are

Table III

Micropunctate fluorescein staining in a series of normal eyes and in a pathological material after instillation of 0.125% fluorescein or 1% fluorescein combined with 1% rose bengal

dye	clinical condition	Punctate fluorescein staining percentage number of corneae							
		none*	1-4*	5-9†	10-24*	25-99*	100-999*	≥ 1000*	number of eyes
0.125% fluorescein	normal	93	9	4	3	1/2	1	0	411
0.125% fluorescein	pathol	41	10	6	18	10	8	8	125
1% flu rose bengal	normal	27	16	2	4	0	16	35	49
1% flu rose bengal	pathol	18	12	3	22	4	19	21	67

* Number stated of minute dots per cornea

Site

In the presence of many minute dots these were as a rule evenly scattered over the whole cornea. Few dots on the other hand were accumulated within a certain limited area most often inferiorly close to the limbus or nasally at the limbus or below and nasally at the corneal limbus (fig. 2)

The dots were diffusely present in 20 per cent of all who displayed micropunctate fluorescein staining

In 62 per cent the dots were situated inferiorly nasally or in between

The dots were rarely found grouped temporally superiorly or centrally on the cornea (table V)

The sites of the dots were independent of the dye solution used and also seemed to be independent of the diagnostic group

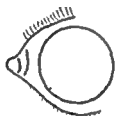


Fig. 2

Example of typical localized micropunctate fluorescein staining of the cornea

Table I

Sites of micropunctate fluorescein staining on the cornea (normal and pathological cases) percentage distribution.

diffusely	20
nasally	10
inferiorly	39
below and nasally	13
temporally	2
centrally	5
superiorly	5
mixed	9

Table IV

Pathological material examined for micropunctate fluorescein staining of the cornea.
Number of corneae examined

	fluorescein 0.125 %	comb 1 % fluorescein and 1 % rose bengal
contact lens wearers	6	12
keratitis	4	16
keratoconjunctivitis sicca	4	11
corneal dystrophy	3	2
corrosion foreign body	7	7
corneal opacity	3	0
chron simple conjunctivitis	26	14
infectious conjunctivitis	7	5
glaucoma	33	1
other	22	8
Total	125	67

Other comprise aphakia pterygium papillomatous conjunctivitis chemosis exophthalmos chalazion phthisis facial nerve palsy iritis

not supposed to involve the cornea than in normal eyes though with a fairly small number on the individual cornea e.g. in chronic simple conjunctivitis

Eyes with infectious bacterial conjunctivitis showed similar conditions as normal eyes

Contact Lens Wearers

Six had 0.125 % fluorescein instilled. In one no micropunctate staining was seen and in one more than 1000 dots while the remaining showed between 5 and 100 dots (Ages 19-57 average 35)

Twelve had a 1 % rose bengal fluorescein mixture instilled. They all presented minute dots three less than 25 dots and five more than 1000 one of the latter as many as about 10^5 (Ages 18-58 average 36)

Rubbing

Intense rubbing on closed lid may provoke micropunctate fluorescein staining. In some instances up to 30 dots could be elicited while in others no such were visible even after repeated rubbing

Such defects were most frequent among the elderly subjects suggesting that the corneal epithelium becomes increasingly vulnerable in the course of years

In a previous study (Aorn 1969) I noticed that the precorneal film bursts sooner in women than in men (wetting time on an average shorter in women than in men)

This poorer protection of the female cornea might be conceived to result in a more frequent occurrence of micropunctate fluorescein staining among women In the series under review no significant difference was demonstrated however

Grantall as early as 1931 showed that the absorption through the cornea is greatly promoted by corneal defects Presence of minute fluorescein stainable defects possibly renders the corneal epithelium barrier less resistant so that accordingly locally applied substances are much more readily absorbed in normal eyes with such defects than in other normal eyes having no defects

The results of the present investigation suggest that a minor proportion of the microdefects are within the physiological range and that these occur particularly in elderly individuals

The phenomenon makes it difficult to distinguish between definitely pathological punctate fluorescein staining and physiological micropunctate staining

The smaller the number of minute fluorescein dots the older the patients and the higher the fluorescein concentration used the greater is the probability that the staining may be regarded as being within the physiological range

If on the other hand many minute dots are seen especially in a fairly young individual the finding is to be characterized as pathological (After instillation of 0.1% fluorescein over 100 dots were seen in no normal individual under 60)

In a contact lens wearer micropunctate fluorescein staining must be claimed in practice to be a sign of interrupted continuity of the cornea a defect which may constitute the point of entrance of infection The staining is therefore a danger signal

Unfortunately normal cornea exist having a small number of such defects These defects will naturally persist when contact lenses are worn

On noticing micropunctate fluorescein staining in contact lens wearers a cause of this must be searched for If the stainability cannot be eliminated by changing contact lens insertion technique or wearing time the phenomenon may be no more than a physiological microstaining

As however it is impossible to decide whether this is so the patient will have to remain under control

Rose Bengal Staining

Rose bengal stains degenerated epithelial cells and mucus

Fluorescein stains epithelial lesions the interrupted continuity allowing the dye solution to penetrate and diffuse among the epithelial cells sometimes right into the aqueous humour Hence some areas are only stained by rose bengal and others only by fluorescein (*Norn 1964 B*)

Accordingly the present material presented areas stained by rose bengal alone but with absolutely no fluorescein stained dots in this areas

Conversely in a case of slaked lime corrosion no rose bengal staining nor true fluorescein staining was observed 48 hours after the corrosion whereas numerous minute fluorescein dots were seen at a site corresponding exactly to the corroded area and limited to this

In rare cases only did rose bengal staining and micropunctate fluorescein staining occur within the same area

The site of the minute dots bore no relation to Hudson Ståhl's line

Discussion

Similarly as ordinary fluorescein staining is due to interrupted continuity of the cornea micropunctate staining is supposed to be due to a defect of the corneal surface

Fluorescein diffuses rapidly from the micro lesion to the surrounding part of the cornea thereby rendering an estimation of the size of the defect impossible

The dots are so minute that they must be supposed to be due either to dropping out of a single cell or to a defect between two epithelial cells which allows dye to penetrate into the intercellular space

The present investigation showed that such defects by no means are rare even among normals but that they often are only detectable by use of an accurate and careful technique

The defects were visible in the greatest number after staining with a 1% rose bengal fluorescein mixture This was due to the higher fluorescein concentration in this solution and perhaps also to the fact that simultaneous instillation of rose bengal may cause irritation and possibly provoke hole formation

On the other hand defects were also found in normals after instillation of 0.125% fluorescein to which no other substances had been added and which caused no irritation

Addition of oxibuprocaine (novesin) or a preservative (0.0025% phenylmercuric nitrate) did not raise the number of minute dots

Such defects were most frequent among the elderly subjects suggesting that the corneal epithelium becomes increasingly vulnerable in the course of years

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The results of the present investigation suggest that a minor proportion of the microdefects are within the physiological range and that these occur particularly in elderly individuals

The phenomenon makes it difficult to distinguish between definitely pathological punctate fluorescein staining and physiological micropunctate staining

The smaller the number of minute fluorescein dots the older the patients and the higher the fluorescein concentration used the greater is the probability that the staining may be regarded as being within the physiological range

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As however it is impossible to decide whether this is so the patient will have to remain under control

Summary

Microdefects of the surface of the corneal epithelium were detected after staining with 0.125 % fluorescein in 17 per cent out of 411 normal eyes and after staining with 1 % fluorescein combined with 1 % rose bengal in 73 per cent out of 49 normal eyes.

After instillation of 0.125 % fluorescein only few dots were counted (over 100 in 1 per cent of all the normal eyes). After combined fluorescein and rose bengal on the other hand more than 1000 dots were found in 35 per cent.

The incidence of micropunctate staining and the number of dots were seen to rise with increasing years.

Among the pathological cases micropunctate staining was more frequent and the number of dots greater particularly so in the presence of corneal lesions but also in other cases e.g. chronic simple conjunctivitis.

The point of transition from physiological punctate staining to pathological fluorescein staining is indefinite and renders assessment difficult e.g. in the cases of contact lens wearers. Micropunctate fluorescein staining is however always a danger signal.

References

- Fenton P. J. Applanation tonometry using anaesthetic fluorescein mixture. *Brit J Ophthalmol* 49: 504 (1965).
- Gronwall Herman. Citric acid studies referring to the eye. *Acta Ophthalm. suppl.* VI pp. 279 (1937).
- Norn M. S. Fluorescein vital staining of the cornea and conjunctiva. Studied by triple staining with fluorescein, rose bengal and alcian blue. *Acta Ophthalm.* 42: 1038-1046 (1964A).
- Norn M. S. Vital staining in practice. *Acta Ophthalm.* 42: 1046-1053 (1964B).
- Norn M. S. Desiccation of the precorneal film. I. Corneal Wetting Time. *Acta Ophthalm.* 47: 865-880 (1969).

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GLAUCOMA AND RIEGER'S SYNDROME

BY

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Most cases of iridocorneal dysgenesis suffer from glaucoma or eventually develop high intraocular tension (Pirger 1935 Braendstrup 1948 Kittel 1956 Busch *et al* 1960 Frandsen 1963). In the numerous reports already available the elevated intraocular pressure has been ascribed to an obstruction of the filtering angle by abnormal tissue of mesenchymal origin. A report is made of 2 patients one with a typical syndrome and glaucoma and the other whose glaucoma was mainly due to an angle closure mechanism.

Case 1

In August 1968 a young recruit aged 19 1/2 years was referred to the eye clinic because of ocular pain and headaches after reading. The left eye was weak since birth when it appeared to have an eccentric pupil. Two years before the patient had an abdominal operation due to diverticulitis of the small intestine. The parents and younger brother were normal. Visual acuity was 6/6 in the right eye with a -1.50 sph correction and 6/30 in the left eye. The corneas measured 9 mm vertically and 10.0 mm horizontally. Applanation tonometry gave readings of 34 mm Hg in the right and of 37 mm Hg in the left eye. Both anterior chambers were of normal depth. In the right eye the anterior leaf of the iris was extremely atrophic and the pupillary sphincter stood out like a ring. The pupil was pointed temporally and reacted sluggishly to light. There were several broad bridges of iris tissue attaching to the periphery of the cornea which showed a thickening in the periphery of Descemet's membrane (Fig. 1 RE). Gonioscopy demonstrated a slightly protruding Schwalbe line, the already described abnormal iris attachments which also were connected in some areas to the root of the

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Fig 1

Right eye of male aged 19½ with atrophy of the anterior leaf of the iris displaced posterior embryotoxon and broad adhesions between the iris stroma and the peripheral cornea

Left eye of same patient - iris atrophy The pupil is drawn and temporally Note broad adhesions between the iris stroma and the peripheral cornea

trabecular meshwork and an abnormal greyish opaque tissue covering the angle of the anterior chamber which was open and of intermediate depth

In the left eye the iris was also atrophic The pupil was drawn down and temporally and bridges of abnormal tissue connected the periphery of the iris to the Schwalbe line and to the peripheral cornea from 2 to 7 o'clock (Fig 1 LE) Gonioscopy showed an open angle of intermediate depth A prominent Schwalbe line was present The angle was covered by an avascular structure of characteristics similar to the right eye The broad iridocorneal adhesions were seen at 2 30 to attach also to the root of the trabecule

The media and fundi were normal except for superior and inferior crescents adjacent to the discs The right visual field was normal and the left could not be charted

On the basis of the malformation involving the angle of the anterior chamber iris stroma and peripheral cornea including abnormal strands of iris attaching to the trabecule and in the periphery of the cornea to a posterior embryotoxon the diagnosis was made of a dysgenesis mesodermalis cornea et iridis or Rieger's syndrome

Treatment consisting of 2% pilocarpin drops d.s. and Eppy 1% b.d. in both eyes succeeded in controlling the intraocular pressure An optic iridectomy was performed in the upper temporal quadrant of the left eye This improved the visual acuity to 6/5

Case 2

A 47 year old male was referred to the eye clinic because of iridocorneal dysgenesis and elevated intraocular pressure in both eyes The main clinical symptoms were frontal headaches and transient attacks of ocular pain and redness accompanied by blurred vision especially in the left eye for the last 6 months

The examination revealed a visual acuity of 6/6 in each eye The right cornea measured 10.0 mm × 10.0 mm and the left 9.5 mm × 9.5 mm A marked posterior embryotoxon was present in both sides Atrophy of the iris stroma was present bilaterally Broad iridocorneal adhesions were seen peripherally in both eyes In the right eye there was in addition a tangential band of iris tissue extending from 2 30 to 6 30 and attaching to the cornea in its center (Fig 2) The pupils were pointed downwards



Fig 9

Right eye of male aged 49 Note atrophy of anterior leaf of iris broad adhesions between iris and displaced posterior embryotoxon and fibrous iris and from 2 30 to 6 30 adhering in its central part of the cornea

Left eye of same patient Similar iris atrophy and broad adhesions between iris and peripheral cornea

and reacted very poorly to light in both sides Applanation tonometry revealed tensions of 40 mm Hg in the right and of 50 mm Hg in the left eye After a mydriatic instillation the tension rose by 10 mm in each eye Both anterior chambers were very shallow

The lenses presented pinpoint opacities The vitreous and funds were normal Visual fields were not impaired

Gonioscopy performed when the intraocular pressure was high revealed almost completely closed angles in both eyes Only a small nasal and lower segment could be seen of each angle up to the scleral spur After 2% pilocarpin drops the pressure dropped to 22 mm in the right and to 20 mm in the left eye Repeated gonioscopy under the miotic influence revealed open angles up to the scleral spur In both angle recesses there was a brownish cob web like structure with whitish dots A few irido corneal adhesions were seen attaching to the scleral spur

Treatment consisted of peripheral iridectomies in each eye to treat the closure angle component in this case of iridocorneal dysgenesis After surgery the tension was regulated with pilocarpin 2% twice daily

DISCUSSION

Rieger's syndrome is a mesodermal developmental abnormality consisting of iris hypoplasia especially of the anterior layers and abnormalities in the angle of the anterior chamber produced by a more or less marked abnormal tissue and by strands of iris adhering to a posterior corneal embryotoxon Associated with the syndrome different systemic abnormalities due to ectodermal mal development have been reported (Hagedoorn 1937 Henkes 1965) Most of the affected patients have or will eventually develop glaucoma The elevated intra ocular pressure has always been linked to the abnormal tissue blanketing the

filtering angle, the more severe the angle dysgenesis causing the more severe glaucoma although glaucoma is known to be present also in milder forms of Rieger's syndrome (Pearce and Kerr 1965). Although the malformation is congenital, glaucoma usually develops later in life in distinction to congenital glaucoma or buphthalmos.

Case 1 in this report represents a typical case in which the abnormal tissue in the angle has produced a juvenile glaucoma.

In Case 2 a middle aged patient the glaucoma was of different characteristics. The angle of the anterior chamber in this patient, was not obstructed by an obvious abnormal tissue. It was mainly an angle closure mechanism which caused the elevated pressure. This was demonstrated gonioscopically by examining the angle under elevated and normal tension. Although the mechanism of this angle closure is not clear, it seems possible that the extensive adhesions bridging the root of the iris to the periphery of the cornea in both eyes could have pulled the iris forward causing shallow anterior chambers. Such a mechanism has also been postulated by Reese and Ellsworth. The moderately mydriatic pupils whose motility was defective might have caused a relative pupillary block. These 2 components could well have played an important role in the mechanism of glaucoma. Peripheral iridectomies eliminated the closure angle component of the glaucoma probably by interfering with the pupillary block component.

Summary

A report is made of 2 patients affected with iridocorneal dysgenesis (Rieger's syndrome).

Case 1 was a typical case in which the juvenile glaucoma was due to blanketing of the filtering angle by abnormal mesodermal tissue.

In Case 2 no obvious abnormal tissue obstructed the filtering angle. Glaucoma developed in middle age mainly due to a closure angle mechanism. It is probable that the closure of the angle was produced by the iridocorneal adhesions pulling forward the iris and by a pupillary block component due to relative mydriasis and poor pupillary motility.

References

Braendstrup J M (1948) Posterior Embryotoxon in Three Generations. *Acta Ophthalmol* 26: 495.

- Busch G Weiskopf J & Busch K T (1960) Dysgenesis mesodermalis et ectodermalis Rieger oder Rieger'sche Krankheit *Klin Mbl Augenheilk* 136 519
- Frandsen E (1963) Rieger's Syndrome Combined with Oligodontia and Finger Deformity *Acta Ophthalm* 41 757
- Hagedoorn A (1937) Congenital Anomalies of the Anterior Segment of the Eye *Arch Ophthalm* 1, 993
- Henkes H H (1965) Acquired Corneal Dystrophy *Brit J Ophthalm* 49 571
- Kittel V (1956) Beobachtungen bei familiar auftretender Irisatrophie mit Drucksteigerung *Klin Mbl Augenheilk* 199 464
- Pearce W C & Kerr C H (1965) Inherited Variation in Rieger's Malformation *Brit J Ophthalm* 49 530
- Pease B R & Ellsworth R M (1966) The Anterior Chamber Cleavage Syndrome *Arch Ophthalm* 75 307
- Rieger H (1935) Beiträge zur Kenntnis seltener Missbildungen der Iris Albrecht v Graefes *Arch Ophthalm* 133 609

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References

- Braendstrup J M (1948) Posterior Embryotoxon in Three Generations. *Acta Ophthalmol* 26 495

present one might be due to fresh mutations or more probably to the well known variation in penetrance of the particular gene. The reasons for this variation in penetrance are not known but genotypic factors such as suppressive or otherwise interacting genes as well as promoting or suppressing environmental factors are to be considered.

The strong hereditary influence on the tumour development has motivated cytogenetical analysis of cultured normal fibroblasts or/and leukocytes from patients with retinoblastomas and sometimes also of their relatives (4-7). No karyotypic deviations from normal have been found in these instances except in one case (4). This patient a 10 month old girl belonged to the category of sporadic cases and chromosomal analysis disclosed a deletion of the long arm of one of the D group chromosomes probably a no 15. This aberration was found in all cells analyzed from cultures of conjunctival and dermal tissue blood cells as well as tumour tissue. In explants of tumour tissue there was in addition an unusually high number of cells with chromosome numbers of 40 or less but with no consistent pattern. No exact counts or karyotypes were given nor any information about the duration of the cultures.

To my knowledge this is the only cytogenetical analysis of a retinoblastoma and it should be observed that the chromosomes were studied only in tissue culture explants. To avoid the potential risks of chromosomal changes during culture direct fixations from the tumour were primarily used in the present analysis. First aim of the present study was to look for whether the deleted D chromosome of Lele et al (4) would be found. Second the chromosomal picture was analyzed in relation to the remarkable hypodiploid pattern reported by Lele et al. Third the findings were compared with those obtained from chromosomal studies of some histologically related tumours.

Material and Methods

The present sporadic case concerned a girl 1 year and 10 months at the time of operation. Strabismus and a greyish right pupil had been noticed for at least 4 months prior to operation. The right eye was found to contain a tumour. Macroscopic examination of the enucleated eye revealed a bulging yellow white tumour which had replaced the corpus vitreum. The histological picture was that of a poorly differentiated retinoblastoma (Fig 1a) which only in small areas showed a tendency towards rosette formation (Fig 1b). Mitotic figures were numerous and some of the anaphases were abnormal with lagging chromosomes and/or multipolarity. There was no scleral infiltration or extension along the optic nerve.

For chromosome preparation small pieces of the soft tumour tissue were finely minced with scissors suspended in Parker's medium 199 and incubated at 37°C for 4 and 8 hours respectively. Colcemid (CIB 1) was added to a final concentration of 1 µg/ml for the suspensions harvested after 4 and 8 hours and to a concentration of 0.2 µg/ml

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CHROMOSOMAL ANALYSIS OF A HUMAN RETINOBLASTOMA

BY

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Summary

The chromosomes of a sporadic human retinoblastoma were studied in fixations directly from the tumour. The karyological picture was characterized by the following features: hyperdiploid stem sidelines with characteristic marker chromosomes, a restricted spread around the stemline number and some polyploid mitoses. The findings differed completely from the inconsistent pattern reported for another sporadic retinoblastoma investigated exclusively after explantation *in vitro*. In this previously described retinoblastoma a deletion affecting one of the long acrocentrics was found both in normal and tumour cells. This deletion was not seen in the present case.

A comparison was made with chromosome conditions reported from medullo- and neuroblastomas without finding any obvious similarities.

In vitro investigations of the present retinoblastoma indicated an early and gradual substitution of the tumour cells by stroma cells.

Introduction

The development of human retinoblastomas is believed to be dependent on the presence of a single dominant gene. The occurrence of sporadic cases as the

for that taken after 8 hours. Hypotonic treatment was performed by adding 5 parts distilled water to 1 part suspension. After 20 minutes the suspension was centrifuged, the supernatant discarded and 60 per cent acetic acid 0.1 N hydrochloric acid fixative added for 90 minutes. The pellet was then stained in 2 per cent orcein and squashes made on siliconized slides. All counts of metaphase were repeated 2 or more times. Karyotype analyses were made by photography.

Pieces of tumour tissue were also explanted *in vitro* using milk dilution bottles and Parker's medium 199 supplemented with 10 per cent unfiltered inactivated calf serum. Chromosomal preparation was performed as described above except for a somewhat weaker hypotonic treatment.

Results

1 Numerical Findings

The chromosomal findings in the three consecutive fixations directly from the tumour showed no differences and the results were pooled in Table I. As seen from this table there was a sharp mode at 47, the stemline (S) number. The spread around the S number was moderate and restricted to $S \pm 3$ but the distri-

Table I
Chromosome number distribution: a sharp mode at 47

Chromosome numbers																	Total
44	45	46	47	48	49	50	51	78	84	85	86	87	88	89	90	91	92
16	9	103	93	5	1	1	1	2	-	1	-	1	-	2	-	1	173

Fig. 1

- Histological picture of the main part of the retinoblastoma. No organoid structures. Haematoxylin-eosin $\times 330$.
- Small area with rosette-like structures adjacent to one with reactive gliosis. Haematoxylin-eosin $\times 330$.
- Metaphase of the stemline $S = 47$. The arrow points at the small m_1 marker $\times 1035$.
- Metaphase of subgroup III 47 chromosomes. The arrow points at the big m_2 -marker 103.
- Part of metaphase of subgroup II. The big arrow points at the t_3 marker and small arrows point at 8 double minutes $\times 4150$.

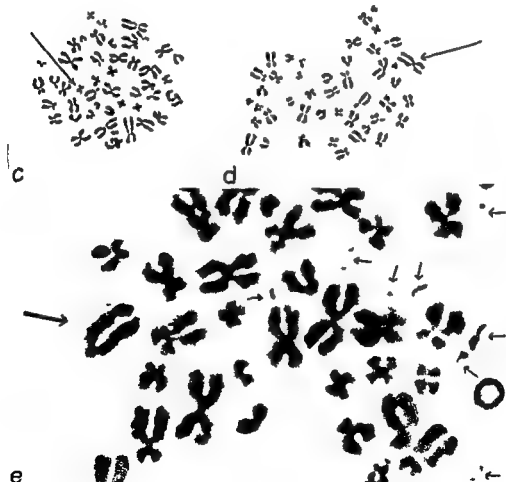
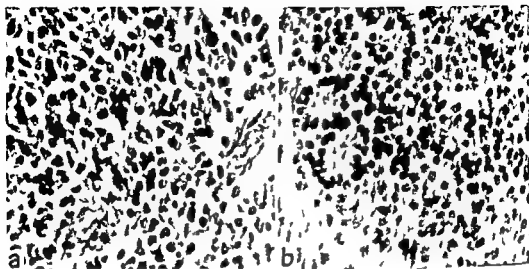


Fig 1

Table II
Kary types of 0 cells presented as deviation from normal female diploid or tetraploid karyotype. Division into three subgroups on the basis of marker distribution (last columns)

Number of chr mosomes	Number of cells	Chromosome groups										Markers			Subgroup	
		1	2	3	4	5	6	7	8	9	10	t ₁	t	m ₁		m
45	1	+1	-	-	+1	-1	-	-	-	-1	-	-	-	+1	-	I
45	3	+1	-	-	+1	-1	-	-	-	-1	-	-	-	+1	-	I
46	1	+1	-	-	+1	-1	-	-	-	-1	-	-	-	+1	-	I
47	1	+1	-	-	+1	-1	-	-	-	-1	-	-	-	+1	-	I
47	4	+1	-	-	+1	-1	-	-	-	-1	-	-	-	+1	-	I
47	19	+1	-	-	+1	-1	-	-	-	-1	-	-	-	+1	-	I
48	7	+1	-	-	+1	-1	-	-	-	-1	-	-	-	+1	-	I
49	1	+1	-	-	+1	-1	-	-	-	-1	-	-	-	+1	-	I
49	1	+1	-	-	+1	-1	-	-	-	-1	-	-	-	+1	-	I
50	1	+1	-	-	+1	-1	-	-	-	-1	-	-	-	+1	-	I
50	1	+1	-	-	+1	-1	-	-	-	-1	-	-	-	+1	-	I
51	1	+1	-	-	+1	-1	-	-	-	-1	-	-	-	+1	-	I
45	1	+1	-	-	+1	-1	-	-	-	-1	-	+1	-	+1	-	II
45	1	+1	-	-	+1	-1	-	-	-	-1	-	+1	-	+1	-	II
46	1	+1	-	-	+1	-1	-	-	-	-1	-	+1	-	+1	-	II
47	1	-	-	-	+1	-1	-	-	-	-1	-	+1	-	+1	-	II
47	1	-	-	-	+1	-1	-	-	-	-1	-	+1	-	+1	-	II
49	1	+1	-	-	+1	-1	-	-	-	-1	-	+1	-	+1	-	II
45	1	-1	-1	-	+1	-1	-	-	-	-1	-	-	-	-	+1	III
46	6	-1	-1	-	+1	-1	-	-	-	-1	-	-	-	-	+1	III
47	1	-1	-1	-	+1	-1	-	-	-	-1	-	-	-	-	+1	III
54	1	-1	-1	-	+1	-1	-	-	-	-1	-	-	-	-	+1	III

Double minutes excluded

bution was asymmetrical due to excess of 48 chromosome cells. About 5 per cent of the counted cells were polyploid. Since it was possible to make exact counts in almost every metaphase detected during the screening and the incidence of evidently broken cells was low, the recorded frequency of polyploids can be regarded as a good estimate of the true frequency. Numerically it was noteworthy that none of the polyploid cells represented a simple doubling product of the stemline.

II Markers

Fifty one metaphases were subjected to detailed karyotype analysis; most cells had the 8 number but several diploid, near diploid and some polyploid variant cells were included. In Table II the karyotyped cells were divided into 3 subgroups according to the distribution of 3 different markers. About 78 per cent of the cells analyzed belonged to subgroup I, characterized by the occurrence of one or in the tetraploids two metacentric markers (m type according to the nomenclature proposed by Levan et al. (5)). This m_1 marker was intermediate in size between pair no. 16 and the biggest pair of nos. 19-20 (Fig. 1c, 2, 3a and b). Subgroup II encompassed about 12 per cent of all metaphases analyzed; in addition to the m_1 marker described above, all cells showed an acrocentric marker (t type). At the same time one nos. 13-15 was missing in 4 of the 6 cells analyzed. This t_1 marker was almost twice as long as the longest pair in the group nos. 13-15 and it had a vague secondary constriction in the middle of the long arm (Figs. 1e, 3a and b). Subgroup III, with about 10 per cent of the cells, had no m_1 or t_1 marker but a big metacentric marker (m type); here one no. 1 was missing in all cells. The m_2 marker was similar to pair no. 9 with regard to arm index but both arms were about 25 per cent longer than those of pair no. 2 (Figs. 1d, 3c). The three described markers m_1 , t_1 and m_2 had the same morphological appearance and relative size in different cells within each of the subgroups.

Other types of markers were seen only in two cells, both belonging to the second subgroup (Table II). In one 46 chromosome cell there was a small acrocentric marker t , half as big as the smallest pair of the G group (Fig. 3b). The other cell had 45 chromosomes including the m_1 and t_1 markers and in addition 8 or possibly 9 minute chromatin bodies (Fig. 1e). The size of some of them was at the border of visibility which accounted for their reduced stainability. They clearly had two chromatids which often were more separated than in ordinary chromosomes. At least some of the minutes seemed to be centric. In all their characteristics they agreed with the double minutes in some Rous mouse sarcomas (8) and they will be termed double minutes here too.

The two cells with deviating marker sets did not influence the general picture of the distribution of m_1 , t_1 and m_2 markers. The impression that the

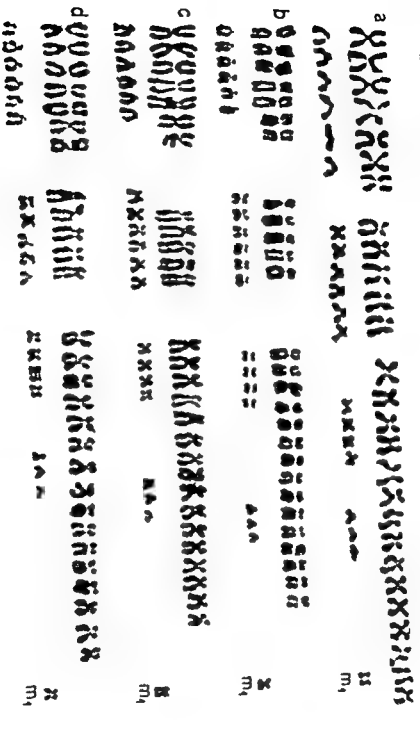
bution was asymmetrical due to excess of 48 chromosome cells. About 5 per cent of the counted cells were polyploid. Since it was possible to make exact counts in almost every metaphase detected during the screening and the incidence of evidently broken cells was low, the recorded frequency of polyploids can be regarded as a good estimate of the true frequency. Numerically, it was noteworthy that none of the polyploid cells represented a simple doubling product of the stemline.

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marker. The chromosomes grouped according to the Denver classification $\times 2190$ f_{10}^0 one m_1 marker and d the sideline $s = 47$ one m_1 marker $S = 47$ one m_1 marker e the sideline $s_1 = 48$ one m_1 marker and b the sideline $S = 47$ one m_1 marker. The chromosomes grouped according to the Denver classification $\times 2190$

tumour cell population was composed of three different subgroups of cells was further strengthened by the numerical variation within each group

III Karyotypes of Stem Sidelines and Variant Cells

Twenty three of the 24 analyzed cells with 47 chromosomes belonged to subgroup I and 19 of them had identical karyotype. In addition to the m_1 marker this karyotype was characterized by an extra of each no 1 and nos 4 and a loss of one nos 6 Δ -12 and one nos 21 22 (Figs 1c 2a and b). These cells constituted the stemline. Since the 47 chromosome cells were random samples, it can be calculated that almost 50 per cent (49.4 per cent) of the counted tumour cells belonged to the stemline (Tables I and II). The other four 47 chromosome cells of subgroup I all differed from the stemline by loss of one nos 17-18 instead of one nos 6 Δ 12 (Fig 2c). A similar calculation of the incidence in the tumour cell population of this particular karyotype gave a frequency of about 10 per cent (10.4 per cent). These cells were regarded as a sideline (s) according to the nomenclature adopted in previous investigations (c g 8) a minimum of 10 per cent of a certain karyotype was required for this designation. A second somewhat more prominent sideline was found in subgroup I having 48 chromosomes and differing from the S by having the normal number of 6 Δ 12 chromosomes (Fig 2d). All 48 chromosome cells analyzed belonged to this sideline which had an estimated frequency in the tumour cell population of about 13 per cent (13.3 per cent).

The rest of the diploid near diploid cells of subgroup I were evidently variant cells closely related to the stem sidelines though their exact mode of origin could not be determined. The same was probably true of the few tetraploid cells but most of them seemed to have undergone secondary changes after the doubling of the chromosome number.

No definite sidelines could be identified in the other two subgroups II and III. However the cells within each group showed great similarities both in numerical and structural variation. Thus it might be justified to regard each of the small subgroups as a counterpart to a sideline probably having similar importance in the population dynamics. The karyological findings in both subgroup II and III indicated that they were derived from subgroup I.

Though the origin of the m_1 marker could not be traced with certainty the situation was somewhat different for the t_1 and m markers. Thus as pointed out in a previous section the t_1 marker appeared at the same time as one nos 13 15 was lost in 4 of 6 karyotyped cells. It seemed reasonable to assume that the t_1 marker represented a remodelled long acrocentric. Analogously the m marker might well be derived from a chromosome no 1 one or two chromosomes no 1 were missing in all cells of subgroup III.

The frequency of breakage was only about 5 per cent in all fixations and

none of the markers were ever affected. Thus it is reasonable to assume that the markers were formed early in tumour development creating conditions for a fairly long period of stabilization of the newly formed chromosomes. The morphological constancy and lack of any appreciable variation in size at the time of fixation were characteristics of the markers supporting this assumption.

IV In Vitro Results

The development of the material explanted *in vitro* was followed continuously in the inverted microscope. During the first week the cells attached to the wall consisted of small uniform elements arranged into loose sheets. These cells rapidly degenerated during the following week and the few cells left were larger and spindle shaped. They grew very slowly and it was not possible until 70 days after explantation to make fixations for chromosomal analysis. At that time the cells formed sheets but contact inhibition was preserved.

Only one fixation was successful and among the 30 countable metaphases 27 had 46 chromosomes and 8 had 92 chromosomes. All karyotypes were normal female diploid or tetraploid. Thus both cell morphology and chromosomal analysis indicated that the finally outgrowing elements represented stroma cells. It could not be decided whether the comparatively high frequency of tetraploid cells was a characteristic of the stroma cells explanted or a response to the *in vitro* conditions.

Discussion

The present retinoblastoma differed in chromosomal picture from the retinoblastoma reported by Lele et al (4). Instead of an inconsistent hypodiploid pattern the present case was characterized by a well defined hyperdiploid stem line and two small sidelines both closely related to the stemline. About 3/4 of the tumour cell population belonged to the stem sidelines and the variant cells showed a pattern of karyotypic deviations deducible from the stemline.

No deletion of a D chromosome was noticed in the present case either in the tumour cells or in the normal cells growing in the tissue culture. Thus the present case does not support the thought of Lele et al (4) that sporadic retinoblastomas may develop as a consequence of the hemizygous condition of a D chromosome segment specifically involved in the formation of these tumours. Thus the localization of the gene for development of retinoblastomas remains uncertain. Investigations of further cases might elucidate this question as also the possible genic control of the karyotypic evolution in the retinoblastomas.

Histologically the retinoblastomas are very similar to two other types of neu

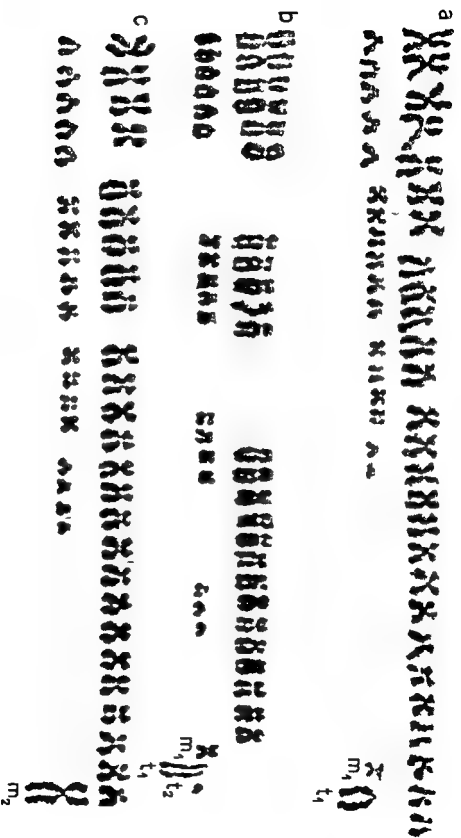


Fig. 3

karyotypes of variant cells from a subgroup II 46 chromosomes one m_1 marker and one t_1 marker b subgroup II 46 chromosomes one m_1 one t_1 and one t marker and c subgroup III 45 chromosomes one m marker \times 2190

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rogenic tumours the medulloblastomas and the neuroblastomas. Comparatively few of each type have been studied chromosomally (1, 3, 11 and references in 8) and among those reported there is a variety of cases with a seemingly normal diploid stemline and also with an abnormal either diploid near diploid or polyploid stemline. None of them shows any clear karyotypic similarities to the present case. However some of them belong to the restricted category of human tumours showing the structural aberration termed double minutes. As pointed out earlier one of the studied 173 cells of the present retinoblastoma showed this aberration. Since the phenomenon has been observed in one or a few cells of several astrocytic gliomas (2, 11) and some gastrointestinal carcinomas (12) it might be that this aberration is more common than apparent from the reports though it is still believed that an engagement of a major part of a tumour cell population is definitely a rare event.

Recent studies of human and animal tumours have demonstrated a correlation between pathological parameters and chromosomal findings (for review see (10)). Consequently it is interesting to note that the considerable karyotypic remodeling in the present retinoblastoma was paralleled by a poorly differentiated histological character. The formation of rosettes is regarded as a characteristic of more mature tumour types with a less severe prognosis. Further cases will reveal if these more mature types have a correspondingly more normal chromosomal picture.

The inability to establish a tumour cell culture during prevailing *in vitro* conditions is apparent. The stromal replacement which already seemed to start during the second week was a phenomenon in line with findings in Rous virus induced sarcomas of the mouse (9). In view of the uncertainty as to what cells grow out in tissue culture it is definitely safer to make the chromosomal analyses on direct fixations from the tumour whenever possible. As a rule only fixations from real short term cultures (3) may be regarded as a reliable substitute or complement to the direct fixations.

Acknowledgements

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References

1. Erkmann B & Conen P E (1961) Chromosome constitution of 14 human malignant tumours. *Proc Am Ass Cancer Res* 5: 17.

- 2 Hansteen I L (1967) Chromosome studies in glial tumours Europ J Cancer 3 183
- 3 Kotler S & Lubs H A (1961) Comparison of direct and short term tissue culture techniques in determining solid tumor karyotypes Cancer Res 27 1861
- 4 Lele K P Penrose S & Stallard H B (1963) Chromosome deletion in a case of retinoblastoma. Ann Hum Genet Lond 27 171
- 5 Levan A Fredga K & Sandberg A A (1964) Nomenclature for centromeric position on chromosomes Hereditas 50 101
- 6 Levan A Manolov G & Clifford P (1969) The chromosomes of a human neuroblastoma. A new case with accessory minute chromosomes J Nat Cancer Inst In press
- 7 Makino S (1968) Chromosomal screening data in congenital disorders and sexual defects From a survey work in Makino Laboratory 1964 to 1967 Mammalian chromosomes newsletter 9 217
- 8 Mark J (1961) Double minutes - chromosomal aberration in Rous sarcomas in mice Hereditas 57 1
- 9 Mark J (1961) Chromosomal analyses of Rous sarcomas in mice - comparison between the findings in the tumour and in material explanted *in vitro* Acta path microbiol scand 10 37
- 10 Mark J (1968) Relationships of chromosomal and pathological findings in Rous sarcoma virus induced tumours in the mouse Int J Cancer 3 663
- 11 Mark J (To be published) Chromosomal analysis of human astrocytic gliomas
- 12 Miles C P (1967) Chromosome analysis of solid tumours II Twenty six epithelial tumours Cancer 90 1274
- 13 Miles C P (1967) Chromosome analysis of solid tumours I Twenty eight non-epithelial tumours Cancer 90 1023

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THE ERG AND OPHTHALMOLOGICAL CHANGES IN EXPERIMENTAL METALLOSIS IN THE RABBIT

I Effects of iron particles

BY

BENGT KNAVE

Introduction

Retained intraocular iron particles can give rise to changes in the different tissues of the eye called *siderosis bulbi*. Retinal damage often occurs at an early stage and is the most detrimental result of *siderosis*.

After introducing electroretinography (ERG) for clinical purposes *Karpe* (1948 1957) showed that pathological changes in the ERG could be correlated to retinal *siderosis* which finding has been confirmed in other clinical investigations (*Schmager* 1956 *Straub* 1961 *Kozousek* 1965 *Knave* 1969a).

In the last mentioned of these investigations the most case material was presented 68 cases were selected for analysis 42 of which with an intraocular iron particle. Localization duration and degree of encapsulation of the intraocular particles did not explain the differences in the development of *siderosis* from case to case. The results indicated that minor differences in alloy content might play a role.

The clinical results thus pointed to the necessity of an experimental approach in animals. It should be mentioned that the ERG following intraocular im

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plantation of iron pieces has earlier been described in two studies on rabbits (Sugita *et al* 1960 Seto 1960) the results of which were ambiguous Sugita reported that the *b* wave following the implantation of an iron pin either decreased was constant or increased Seto on the other hand found a progressive decrease from day to day The *a* wave and the oscillatory potential were not evaluated ophthalmoscopic findings were not presented and the observation time was too short (one and two months respectively)

In the present investigation the changes in the *a* and *b* waves as well as in the oscillatory potential were studied during a long period (up to 1½ years) after implantation of pure iron particles in the vitreous of the rabbit The investigations were made with a recently described method which was used in studies on long term changes in retinal function induced by high intensity flashes (Knaue 1969b) Moreover ophthalmological examinations were performed the results of which were compared with those of the electrophysiological investigations

Material and Methods

Electroretinogram The method which has been described in detail in a previous work (Knaue 1969b) allowed repeated ERG recordings during a long period of time (in this study 1½ years) in the non anaesthetized rabbit. Due to strictly standardized experimental conditions the normal variations in the *b* wave were small Recordings were made simultaneously from both eyes which were illuminated with equal intensity one eye serving as test object and the other being used as reference The light stimulus consisted of an electronic flash (Braun F 87) the intensity of which could be varied by means of neutral filters In the present experiments the unattenuated flash intensity was used since high stimulus intensities are required to elicit an adequate *a* wave in the rabbit which has an F retina (Granit 1935) and to evoke an oscillatory potential (Yonemura *et al* 1963) The unattenuated flash had an intensity of about 1 log units above the *b* wave threshold of the dark adapted eye The average value of three recordings was used when evaluating the potentials When recording the *a* and *b* waves the first flash was applied to the dark adapted eye and the following flashes were presented with intervals of 10 min The oscillatory potential was obtained in response to flashes which were presented with intervals of 30 sec which provided a suitable photopic adaptation of the retina Different time constants were used in the recording system. When recording the *a* and *b* waves a time constant of 1 sec was used The time constant was 10 msec when recording the oscillatory potential Finally the *a* and *b* waves

were measured from their peaks to the isoelectric line. The B -wave was defined as the total amplitude from the peak of the a -wave to the peak of the b wave.

In this connection mention must be made of the recently reported long term reversible changes in retinal function induced by short high intensity flashes (Anave 1969b c). In these studies it was found that even a single light flash with an intensity of about 7 log units above the b wave threshold of the dark adapted eye was followed by a slight but significant reduction of the b wave, obtained in response to a low intensity stimulus. The reduction was found to last for about a week. One hundred flashes with an intensity of about 9 log units above the b -wave threshold were shown to result in an initial increase followed by a transient decrease of the b -wave, the recovery to pre illumination values being accomplished in about two weeks.

As a consequence of these long term reversible flash effects the value of the test eye was always compared to that of the intact eye. The normal variation of the relative differences between the right and left eye was investigated. Table I shows these differences obtained on 8 rabbits (expressed in per cent of the higher value). Seven to 12 observations were performed in a period of 11 weeks. In table I a plus sign (+) denotes that the right eye had the greater amplitude, a minus sign (—) denotes the opposite condition. Table I also shows the corresponding standard deviations for each animal. On the basis of these data the weighted mean of the standard deviations for a single observation was calculated. Thus the weighted $s_{a_{diff}} = 3.9\%$, $s_{B_{diff}} = 5.0\%$, $s_{b_{diff}} = 6.8\%$. Although the latencies were not evaluated in detail it can be stated that their variation was in the same order of magnitude as that of the amplitudes.

Table I

Normal variation of the differences between right and left eye ERG amplitudes obtained by a high intensity stimulus

Rabbit No	$\bar{a}_{diff} (\%)$	$s_{a_{diff}} (\%)$	$\bar{B}_{diff} (\%)$	$s_{B_{diff}} (\%)$	$\bar{b}_{diff} (\%)$	$s_{b_{diff}} (\%)$
1	—2	5.2	—1	4.1	—1	5.1
2	+2	4.3	0	4.8	—1	7.0
3	—4	4.3	—1	4.0	0	4.3
4	+1	2.9	+1	3.5	+1	5.6
5	—1	3.9	—2	4.3	—3	4.8
6	+2	3.3	—2	6.4	—5	8.9
7	—6	3.6	—8	5.6	—9	6.9
8	0	2.9	11	5.6	0	8.2

It should also be mentioned that the long lasting high intensity flash effects shown by Knafe (1969b c) were of the same relative magnitude in eyes with varying degree of siderotic damage and in intact eyes

Ophthalmological examination The anterior segment of the eye was studied in a corneal microscope The posterior segment and the vitreous was examined by direct and indirect ophthalmoscopy The intraocular tension was grossly evaluated by means of careful palpation with small glass rods in no case there was any appreciable difference between right and left eye Moreover the corneal diameters were checked to be less than 15.16 mm to exclude eyes with glaucoma (Holker *et al* 1966) Photographs of implanted particles were taken with an epitelescope camera (Zeiss)

Implantation technique The iron particles and in one experiment an iron salt solution were inserted (injected) transsclerally into the vitreous of the right eye Lumbar puncture needles (outer diameter 0.90 mm) were used for the scleral puncture when implanting the particles and a hypodermic needle (No. 20 outside diameter 0.45 mm) for the injection of the solution The iron particles were loaded into the tip of the lumbar puncture needle ahead of the stylet and then sterilized by dry heat The needle was inserted just outside the corneal limbus (at about 6 o'clock of its circumference) through the ciliary body and into the vitreous The solution was injected in the upper temporal quadrant of the bulb 7.8 mm from the corneal limbus All intraocular applications were performed in intravenous Narkotal® (Astra) or Nembutal® (Abbott) anaesthesia.

Implanted particles The implanted particles consisted of chemically pure iron (purum FeBO). Each particle had an area of 10.15 mm^2 i.e. the particles were small cubes with a side of 0.405 mm

Results

The electroretinogram following a scleral puncture

The electroretinographical changes following a scleral puncture with a lumbar needle are shown for two animals (A and B) in Fig. 1 The results following a hypodermic needle puncture are shown for one animal in Fig. 2 In the figures the puncture was performed at zero on horizontal time axis The ERG amplitudes (vertical axis) were expressed in per cent of those of the intact fellow eye The pre-experimental relative amplitude values varied around 100 per cent from animal to animal In all the figures of the present study this variation was corrected for i.e. all the pre-experimental values were adjusted to 100 per cent with subsequent correction of the following experimental values.

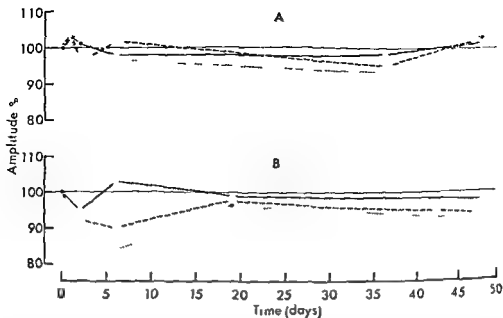


Fig 1

ERG amplitudes (in per cent of those of the intact fellow eye) following a lumbar needle scleral puncture (performed at zero on horizontal time axis) in two rabbits (A and B) Solid line represents the *a* wave dotted line the *b* wave and broken line the *B* wave the latter being defined as the total amplitude between the peak of the *a* wave and peak of the *b* wave

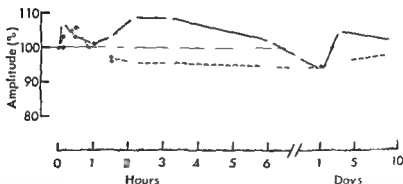


Fig 2

ERG amplitudes (in per cent of those of the intact fellow eye) following a scleral puncture (performed at zero on horizontal time axis) by a thin hypodermic needle Solid line represents the *a* wave dotted line the *b* wave and broken line the *B* wave the latter being defined as the total amplitude between the peak of the *a* wave and the peak of the *b* wave

in all the figures a solid line between filled circles represented the *a* wave a broken line the *B* wave and a dotted line the *b* wave

It is evident that a lumbar needle scleral puncture *per se* might induce a slight reversible reduction of the *B* and *b* waves during the first 12 weeks (Fig 1B) The *a* and *b* wave latencies and the oscillatory potential were not affected The hypodermic needle puncture was followed by insignificant amplitude changes As can be seen in Fig 2 an increase of the *a* wave and a reduction of the *B* and *b* waves were recorded a couple of hours after the puncture and two days later

On ophthalmological examination a slight leakage of vitreous was visible 35 hours following the scleral puncture performed with a lumbar puncture needle Moreover a slight flare in the anterior chamber was visible the first 45 days The scleral puncture by the thin hypodermic needle was not followed by any significant ophthalmological changes

Electroretinographical and ophthalmological changes following intravitreal application III Iron particles

Iron particles were implanted in the vitreous of the right eyes of the rabbits as follows one rabbit received 15 particles two rabbits received 8 particles and two more received 4 particles The first mentioned of these animals was studied for more than three months the others for more than a year In an additional rabbit an iron salt solution was injected intravitreally

Implantation of 15 iron particles In Fig 3 the changes in ERG after implantation of 15 particles are presented Fig 3A illustrates the *a* *B* and *b* wave amplitudes (filled circles) and the scotopic *b* wave peak latency (squares) expressed in per cent of those of the intact fellow eye Fig 3B shows the peak latencies of the five first positive oscillations of the oscillatory potential *v*₁ *o*₁ *o*₂ *o*₃ *o*₄ and *o*₅ marked with triangles When affected these latencies all ways were found to increase compared to the normal latencies of the intact eye In the diagram this increase is expressed in msec

As can be seen in Fig 3A there was a fast initial decrease in the amplitudes After about 5 days this decrease was followed by a small increase and the amplitudes remained at subnormal values during the following month After about 4050 days however a steady decrease was noted until the 100th day when no potentials at all could be recorded

The peak latency of the scotopic *b* wave first temporarily increased This increase corresponded to the initial decrease in amplitude After about 25 days a progressive reduction was recorded After about 60 days however the latency steadily increased to normal values

The latencies of the oscillatory potential increased slightly at first with a

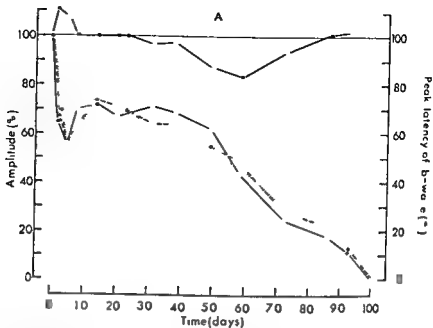


Fig 3A

Amplitudes (filled circles = wave solid line b wave dotted line B wave broken line) and scotopic b wave peak latency (squares) expressed in per cent of those of the intact fellow eye following the implantation of 15 iron particles in the vitreous of a rabbit eye (implantation performed at zero on horizontal time axis)

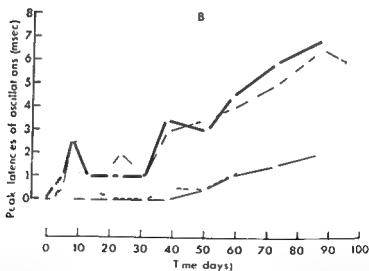


Fig 3B

Peak latencies of the first five positive oscillations (triangles o_1 thin solid line o_2 broken line o_3 dotted line o_4 broken dotted line o_5 heavy solid line) of the oscillatory potential in the experiment described in Fig 3A. When affected these oscillations were always increased this increase is expressed in msec the reference being the intact fellow eye

subsequent normalization after about 10 days. Thirty days later a progressive increase of the latencies started. This increase is illustrated in Fig. 4 which shows the oscillatory potential at three stages of the developing retinal damage (A, B and C in chronological order). The upper tracings were recorded from the test eye and the lower tracings from the intact eye. In Fig. 4A the curves were recorded from an animal in which 8 particles were implanted in the right eye. Here a slight increase of the latencies can be seen and this increase is

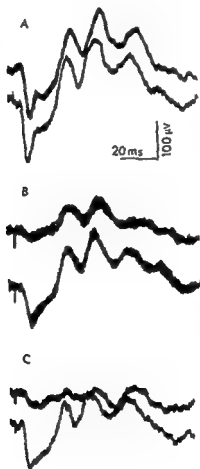


Fig. 4
The oscillatory potential at three stages of developing retinal damage in siderosis bulbi
(A, B and C in chronological order). Upper tracings: test eye; lower tracings:
intact fellow eye.

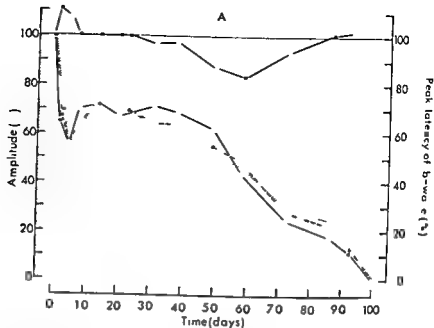


Fig 3A

Amplitudes (filled circles *a* wave solid line *b* wave dotted line *B* wave broken line) and scotopic *b* wave peak latency (squares) expressed in per cent of those of the intact fellow eye following the implantation of 15 iron particles in the vitreous of a rabbit eye (implantation performed at zero on horizontal time axis)

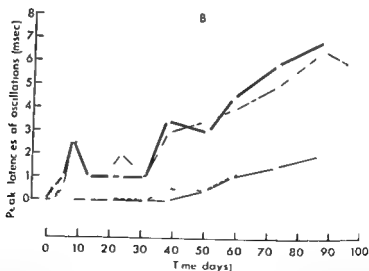


Fig 3B

Peak latencies of the first five positive oscillations (triangles *o*₁ thin solid line *o*₂ broken line *o*₃ dotted line *o*₄ broken dotted line *o*₅ heavy solid line) of the oscillatory potential in the experiment described in Fig 3A. When affected these oscillations were always increased this increase is expressed in msec the reference being the intact fellow eye

weeks after the implantation and may represent an incipient atrophy of the retina

On ophthalmological examination special interest was paid to the vitreal reaction to the implanted particles. This reaction is photographically illustrated in Fig. 5. In all the photographs in this figure rounded intense white spots can be seen. These represent photographic artefacts from reflexes in the lens system. In Fig. 5A the particles were photographed two hours after the implantation: the particles are seen uncovered in the vitreous and one of the white broad of medullary fibers in the rabbit fundus is seen behind. Two days after the implantation (Fig. 5B) an incipient encapsulation of the particles was noted and after 10 days (Fig. 5C) the encapsulation was maximal being formed by a white and diffusely delimited material. From this moment on however the capsule slowly changed its appearance. It became smaller more sharply delimited and changed its colour from white to yellowish white. These capsule changes probably representing a resorption process continued until most of the particles were seen uncovered and glistening again (Figures 5D, E and F are pictures taken 25, 40 and 55 days after the implantation respectively). The development of the initial reversible decrease and the subsequent slow reduction of the ERG amplitudes might be due to changes in the concentration of toxic metal ions (or ion complexes) in the vitreous. In fact this assumption is supported by the ophthalmoscopic findings. Fig. 6 shows that there is a temporal correlation between the electroretinographic changes and the capsule formation and resorption. It is to be expected that the dissociation of the iron ions from the particles is maximal immediately after the implantation. During this phase the amplitude of the ERG diminishes. Then the ion dissociation steadily decreases partly because of the incipient encapsulation of the particles and partly because of the electrochemical equilibrium which is being established between metal area and the surrounding medium. This decreased ion dissociation is the probable cause of the increase of the ERG recorded on the 10th day. Electroretinographically the following period is characterized by a more or less constant amplitude. At the end of this period the particles reappeared as a result of the capsule resorption (D, F). From then on a progressive retinal deterioration occurred as judged by the reduction of the amplitude of the ERG. The falling phase of the curve and the observed slow decapsulation of the particles indicate that the ion dissociation is slow during this phase.

Injection of an iron salt solution into the vitreous. As mentioned above the initial fast ERG changes can be referred to a sudden retinal exposure to a large number of iron ions or iron containing ion complexes originating from the metal after the implantation. It is to be expected that a similar condition after a sudden retinal exposure to a large number of ions should be obtained by the injection of a small quantity of an iron salt solution into the vitreous.

In order to study the initial process more closely 0.1 cc of a 0.12 M solution

more pronounced in B and C which were recorded from the animal in which 15 particles were implanted (in II five curves are superimposed). In this connection mention should be made of the view that the oscillatory potential is generated by reverberating circuits in the outer plexiform and inner nuclear layers of the retina (see e.g. Brown 1968). The *b*-wave is also considered to originate in the inner nuclear layer although generated as a dipole extending through the layer (Arden & Brown 1965). For these reasons it is advisable to evaluate the oscillatory potential only in relation to the *b* wave and no attempts were made to measure minor quantitative differences in these oscillations. In the experiment illustrated in Fig. 3 for instance the oscillations diminished. However there was also a concomitant reduction of the *b* wave. In the final stage before the potentials disappeared the oscillations even dominated the ERG record (Fig. 4C).

The electroretinographical findings illustrated in Fig. 3 indicate that the development of retinal damage consists of two phases *viz.* an initial temporary one followed by a slowly progressive one. The initial changes comprise a reversible amplitude decrease, a reversible increase of the *b*-wave peak latency and a moderate increase in the latencies of the oscillations. The second phase which in this animal appeared after 40–50 days is characterized by a progressive decrease in the amplitudes and a progressive increase in the oscillatory potential latencies. The *b*-wave peak latency first decreased but later reached normal values.

On ophthalmological examination an aqueous flare was noted for the first five days after the implantation but not later. One of the *clinical siderotical* manifestations in the anterior segment is a brownish pigmentation of the iris (see Knave 1969a). This was not found in the present rabbit experiment probably because of the intense brown colour of the rabbit iris which would render such an observation more difficult. Nor were any clinical iris changes such as mydriasis or atrophy demonstrated. Small pigment granules on the anterior surface of the lens were seen in the corneal microscope. These granules appeared after a day or two and remained throughout the observation period. Similar changes on the anterior surface of the lens were also observed for the rabbits in which 8 and 4 iron particles were implanted.

The chinchilla rabbit normally exhibits a visible pigmentation of the retinal pigment epithelium. The choroidal pattern for instance is obscured by pigment when viewing the rabbit fundus ophthalmoscopically. Conspicuous white broad bands of medullary fibers extending from a deeply cupped optic nerve head contribute to a variegated ophthalmoscopic picture. This might be one of the reasons why no pigmentary retinal degeneration – easily seen in humans – were detected. The only pathological finding the functional consequences of which are shown in Fig. 3 was a peripherally more pronounced glistening reflex from the fundus at direct ophthalmoscopy. This finding was first noted about 6

weeks after the implantation and may represent an incipient atrophy of the retina

On ophthalmological examination special interest was paid to the vitreal reaction to the implanted particles. This reaction is photographically illustrated in Fig 5. In all the photographs in this figure rounded intense white spots can be seen. These represent photographic artefacts from reflexes in the lens system. In Fig 5A the particles were photographed two hours after the implantation the particles are seen uncovered in the vitreous and one of the white broad of medullary fibers in the rabbit fundus is seen behind. Two day after the implantation (Fig 5B) an incipient encapsulation of the particles was noted and after 10 days (Fig 5C) the encapsulation was maximal being formed by a white and diffusely delimited material. From this moment on however the capsule slowly changed its appearance. It became smaller more sharply delimited and changed its colour from white to yellowish white. These capsule change probably representing a resorption process continued until most of the particles were seen uncovered and glistening again (Figures 5D, E and F are pictures taken 25, 40 and 50 days after the implantation respectively). The development of the initial reversible decrease and the subsequent slow reduction of the ERG amplitudes might be due to changes in the concentration of toxic metal ions (or ion complexes) in the vitreous. In fact this assumption is supported by the ophthalmoscopic findings. Fig 6 shows that there is a temporal correlation between the electroretinographic changes and the capsule formation and resorption. It is to be expected that the dissociation of the iron ions from the particles is maximal immediately after the implantation. During this phase the amplitude of the ERG diminishes. Then the ion dissociation steadily decreases partly because of the incipient encapsulation of the particles and partly because of the electrochemical equilibrium which is being established between metal area and the surrounding medium. This decreased ion dissociation is the probable cause of the increase of the ERG recorded on the 10th day. Electoretinographically the following period is characterized by a more or less constant amplitude. At the end of this period the particles reappeared as a result of the capsule resorption (D, F). From then on a progressive retinal deterioration occurred as judged by the reduction of the amplitude of the ERG. The falling phase of the curve and the observed slow decapsulation of the particles indicate that the ion dissociation is slow during this phase.

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In order to study the initial process more closely 1 cc of a 0.12 M solution



Fig 5

Photographs of iron particles in the vitreous two hours (A) two days (B) 10 days (C) 25 days (D) 40 days (E) and 55 days (F) after the implantation of 15 iron particles

of ferric chloride was injected intravitreally in a rabbit eye Fig 7 shows the electroretinographical results during the first hour after which time the eye was enucleated for histological examination As can be seen the m wave was

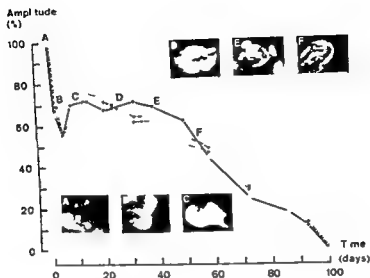


Fig 6

The ERG amplitudes following the implantation of 15 particles correlated to the appearance of the implanted particles. The amplitude graph is taken from Fig 3A and the photographs (A-F) from Fig 5.

first unaffected but decreased slowly later on. The *B* and *b* waves showed similar changes but the decrease appeared earlier and was more pronounced. The peak latency of the scotopic *b* wave was first unaffected but later a minor increase was registered. The latencies of the oscillatory potential did not change very much (see Fig 7B) the amplitudes however continuously decreased and the oscillations were hardly discernible at the end of the experiment. Fig 8 illustrates this amplitude reduction in the upper tracing which represents the test eye practically no oscillations are seen the lower tracing with normal oscillations represents the intact fellow eye.

Implantation of 8 iron particles Eight iron particles were implanted in the right eye of two animals. The results of these two experiments are shown in Fig 9 and 10.

As can be seen in Fig 9 the results of which represent one animal an initial reversible amplitude reduction of the *a* and *b* waves was followed by a slower decrease (Fig 9A). After the 40-50th day however the amplitudes increased again and during the following 300 days remained stationary at the 60-70 per cent level. After 500 days the amplitudes were found to be reduced to about 10 per cent. During the first 60 days the *a* wave reduction was less than that of the *B* and *b* waves. The *b* wave peak latency was slightly diminished up

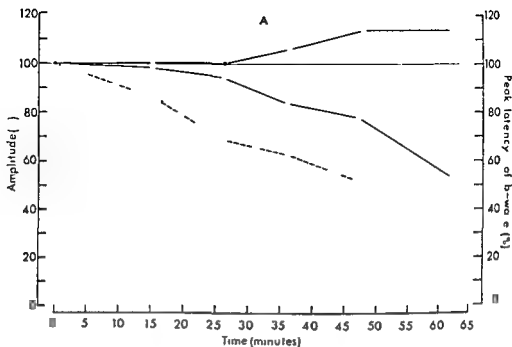


Fig 7A

Amplitudes (filled circles *a* wave solid line *b* wave dotted line *B* wave broken line) and scotopic *b* wave peak latency (squares) expressed in per cent of those of the intact fellow eye following the injection of 0.1 cc of a 0.12 M solution of ferric chloride in the vitreous (injection performed at zero on horizontal time axis)

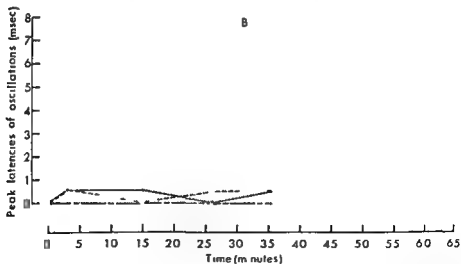


Fig 7B

Peak latencies of the first five positive oscillations (triangles *o*₁ thin solid line *o*₂ broken line *o*₃ dotted line *o*₄ broken dotted line *o*₅ heavy solid line) of the oscillatory potential in the experiment described in Fig 7A. When affected these oscillations were always increased this increase is expressed in msec the reference being the intact fellow eye

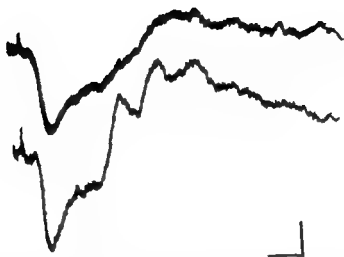


Fig 8

The oscillatory potential recorded from an eye one hour after the intravitreal injection of 0.1 cc of a 0.1% M solution of ferric chloride (*upper tracing*) and at the same time recorded from the intact fellow eye (*lower tracing*) Time marking 10 msec
Amplitude marking 50 μ V

to the 50th day when a relatively rapid decrease was obtained. During the rest of the observation period a normalization and even an increase was noted.

The latencies of the oscillatory potential increased moderately during the two first weeks, reaching a maximum between the 30th and 60th day, followed by a slight decrease (Fig 9B). The reduction of the *a* and *b* waves was also maximal between the 30th and 60th day. Later a progressive increase in the latencies of the oscillations was noted.

Ophthalmoscopically the changes in this eye were similar to those in the eye in which 15 particles had been implanted. Thus the initial encapsulation was followed by a resorption of the capsule causing the particles to reappear. The decapsulation occurred somewhat earlier and was more rapid than in the aforementioned experiment. The glistening fundus reflex seen after 6 weeks in the 15 particle experiment and interpreted as a sign of incipient retinal atrophy was noted after 20-30 days in this experiment. Thus in both experiments described the appearance of the glistening fundus reflex parallels the capsule resorption and is noted only after a prolonged ion exposure to the retina.

When denuded some of the particles were seen to be fragmented. The remains of the capsule were also fragmented into minute parts which were spread

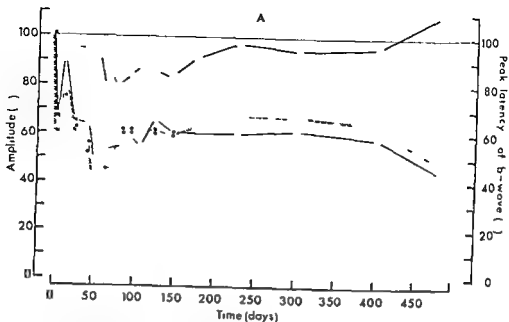


Fig 9A

Amplitudes (filled circles a wave solid line b wave dotted line B wave broken line) and scotopic b wave peak latency (squares) expressed in per cent of those of the intact fellow eye following the implantation of 8 iron particles in the vitreous (implantation performed at zero on horizontal time axis)

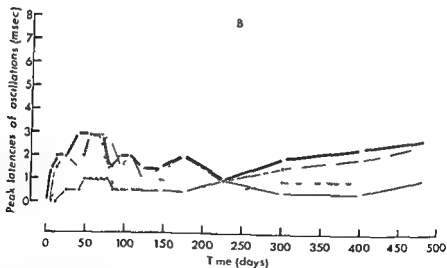


Fig 9B

Peak latencies of the first five positive oscillations (triangles o_1 thin solid line o_2 broken line o_3 dotted line o_4 broken dotted line o_5 heavy solid line) of the oscillatory potential in the experiment described in Fig 9A. When affected these oscillations were always increased this increase is expressed in msec the reference being the intact fellow eye

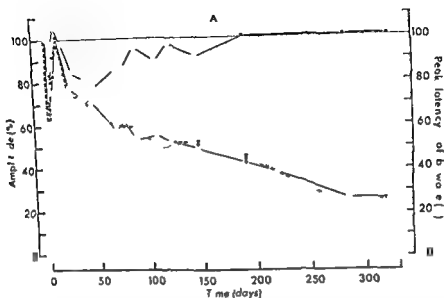


Fig 10A

Amplitudes (filled circles *a* wave solid line *b* wave dotted line *B* wave broken line) and scotopic *b* wave peak latency (squares) expressed in per cent of those of the intact fellow eye following the implantation of 8 iron particles in the vitreous of another rabbit (implantation performed at zero on horizontal time axis)

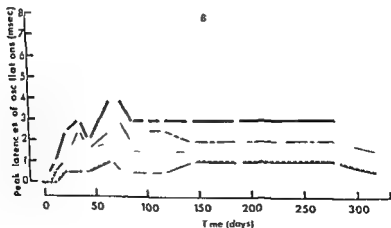


Fig 10B

Peak latencies of the first five positive oscillations (triangles *o*₁ thin solid line *o*₂ broken line *o*₃ dotted line *o*₄ broken dotted line *o*₅ heavy solid line) of the oscillatory potential in the experiment described in Fig 10A. When affected these oscillations were always increased this increase is expressed in msec, the reference being the intact fellow eye.

in the vitreous together with small white wads many of which were lying pre-retinally. In this eye a retinal oedema also developed in a narrow sector peripherally. Therefore a rapid deterioration was expected to follow. Instead an improvement occurred as judged by ophthalmoscopy. The retinal oedema disappeared as did some of the remains of the capsule. It should be mentioned however that some of the preretinal wads persisted followed by local retinal atrophies. The structural improvement which lasted for about a month was paralleled by an increase of the LRG amplitudes between the 60th and 90th day after the implantation (Fig 9A).

The appearance of the particles and their fragments slowly changed in the course of several months. The smallest fragments disappeared entirely and the larger ones very slowly were *encapsulated again*. Thus after about 200 days these particles were seen with a thin and gelatinous capsule. The remains of the initial capsule also changed their appearance to sharply delimited yellow brown structures some of which formed the main parts of strands through the vitreous.

Fig 10 shows the results following the implantation of 8 particles in the other rabbit. The initial changes were similar to those described in Fig 9 but after about 40 days a slow progressive reduction of the *a*- and *b* wave occurred. The changes of the *b*-wave peak latency did not differ much from those illustrated in Fig 9A. The latencies of the oscillatory potential (Fig 10B) showed a normalization trend after about 30-40 days. At about 50 days *c* concurrently with the reduction of the *a* and *b*-wave mentioned above these latencies increased again until about the 100th day whereupon the changes remained stationary for a long time. In the final recording a slight decrease was noted.

Ophthalmoscopically the essential difference between the experiments illustrated in Fig 9 and 10 was the appearance of a large retinal oedema in the latter case. This oedema was visible in a narrow sector 50 days after the implantation. In the course of about a month the oedematous area grew larger to cover a broad sector between 2 and 8 o'clock. This oedema was more or less stationary throughout the rest of the observation period.

Implantation of 4 iron particles Four iron particles were implanted in the right eye of two rabbits. The results of these experiments are shown in Fig 11. No latency data are presented because they did not differ from those of the intact eye. The upper curve (A) representing one of the experiments showed a slight decrease of the potentials the *b*- and *B*-waves being more reduced than the *a*-wave. In the experiment illustrated by the upper curve an incipient encapsulation was noted two days after the implantation. Four days later a delimited vitreal haemorrhage was also seen enclosing the encapsulated particles. This haemorrhage was slowly resorbed and after about 100 days it could not be observed. In its place about 15 small fragments of glistening metal appeared.

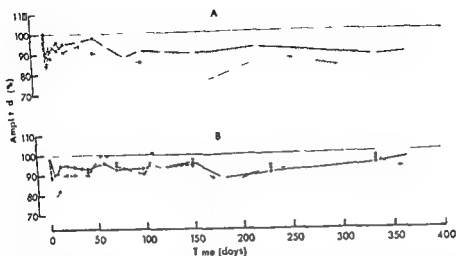


Fig 11

Amplitudes (a wave solid line b wave dotted line B wave broken line) expressed in per cent of those of the intact fellow eye following the implantation of 4 iron particles in the vitreous of the eyes of two rabbits (A and B) (implantation performed at zero on horizontal time axis)

The largest one of these fragments was slowly enclosed by a thin gelatinous capsule. The others lost their glistening appearance and were reduced in number. On the last examination only five very small fragments were seen. A slight amplitude decrease appeared at about 60 days after implantation. This decrease corresponded to the denudation of the metal fragments which probably resulted in an increased iron ion dissociation from the metal to the surrounding media (and thus to the retina). No further damage then occurred probably since the vitreal fluid turn over was now sufficient for the removal of dissociated iron ions from the particles the size of which had been reduced by corrosion.

The lower record (B) of Fig 11 also shows slightly reduced amplitudes but in this respect no difference between the a- and b waves was found. No intravitreal haemorrhage was seen. Encapsulation reactions similar to those described in the 8 particle experiments were observed.

Discussion

The results of this study show that the encapsulation of the implanted particles plays an important role in the development of *siderosis bulbi*. In the first days

in the vitreous together with small white wads many of which were lying pre-retinally. In this eye a retinal oedema also developed in a narrow sector peripherally. Therefore a rapid deterioration was expected to follow. Instead an improvement occurred as judged by ophthalmoscopy. The retinal oedema disappeared as did some of the remains of the capsule. It should be mentioned however that some of the preretinal wads persisted followed by local retinal atrophies. The structural improvement which lasted for about a month was paralleled by an increase of the ERG amplitudes between the 60th and 90th day after the implantation (Fig 9A).

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sent study might well correspond to some of the results presented by these authors. Any comparison of the long term changes however cannot be done because their experiments were carried out during too short a time.

From the results of many investigations (Granit 1933 1947 1955 Noell 1954 Brown & Wiesel 1961a b Arden & Brown 1965 Brown Watanabe & Murakami 1965) the *a* wave has been found to be generated in the photoreceptors and the *b* wave is a dipole extending through both the inner nuclear layer and inner plexiform layer hence the *b* wave probably is generated by the bipolar cells (Arden & Brown 1965). In the clinical studies the first pathological ERG change to appear was that of a type called *neg + 1 e* a pathologically increased *a* wave with a normal *b* wave (Karpe 1957 Knave 1969a). In the subsequent development the *a* wave persisted in most cases while the *b* wave decreased before the ERG became completely non recordable. Thus the clinical investigations indicate that the receptor cells retain function longer than the bipolar cells. This is in agreement with the histological picture of early ganglion cell changes and late receptor cell changes (see e.g. Duke Elder 1954).

That the ganglion cells are destroyed earlier than the receptor cells can be explained by the fact that the metal ions reach the retina from the vitreous and that the parts lying more vitreally are then attacked first. In the present rabbit study no consistent difference between the *a* and *b* wave was found in the eyes in which iron particles were implanted. This might be due to the fact that the rodent retina is thinner than that of man (Detwiler 1943) so that the toxic iron ions reach the ganglion cells and the receptor cells at about the same time. This theory might be supported by the ERG findings immediately after the intravitreal injection of the iron chloride salt solution: the *b* wave was found markedly reduced and the *a* wave more or less intact. The histopathological changes of that eye were mainly found in the neuronal part of the retina with no changes found in the receptor cells (Knave & Lock 1969).

In this connection it should be pointed out that in some of the siderotical eyes of the clinical study (Knave 1969a) both the *a* and *b* wave were found reduced i.e. the ERG was *subnormal*. On the other hand a slowly developing purely negative ERG was also obtained in a rabbit after the implantation of aluminium particles in the vitreous (Knave 1969d). Thus it is very probable that local conditions in the retina and the amount and rate of toxic ions reaching the retina are mainly responsible for the development of the different types of ERG in *siderosis bulbi*. The reaction of different cell types to the metal ions may also be a contributory factor.

It seems reasonable to suggest that the initial changes may be due to a retinal oedema caused by the heavy dose of toxic iron ions reaching the retina. The second slow phase probably is due to a slowly developing retinal atrophy without the involvement of any oedema. Some results of other authors support this suggestion. Thus an amplitude reduction of the oscillatory potential in connec

after the implantation a white and diffuse capsule is produced. This capsule then slowly diminishes and turns yellow. At the same time the particles reappear. First they can be seen as dark spots in the capsule and later the glistening metal is seen. A second thinner capsule appears much later after several months.

To the author's knowledge this double encapsulation process has not been described before. *Leber* (1891) on the basis of experiments on rabbits described the initial encapsulation. On the basis of experiments with rust particles he also described the disappearance of the initial white capsule. It is also known that encapsulated particles after a long time may change their location and then cause inflammation (*Duke-Elder* 1954). It has been claimed that the capsule material is derived from organized hemorrhage and that this material tends to undergo atrophy and dissolution because of the heavy dose of toxic metal ions (*Atlas and Textbook of Ophthalmic Pathology* 1957). This theory is not supported by the results of the present investigation. The present results indicate that the encapsulation process is mainly due to the reaction of the vitreous substance to the particles and is not related to any haemorrhage.

As pointed out the present results indicate two phases in the development of siderotical changes in the retina. The initial phase is probably related to the sudden exposure to the retina of a heavy dose of metal ions immediately after the implantation of the particles and is characterized by the following ERG findings: (1) a partly reversible reduction of the *a*- and *b*-wave amplitudes, (2) a normal or even a slightly increased *b* wave peak latency and (3) a slight or moderate increase of the latencies of the oscillations of the oscillatory potential. In the second phase (1) a slowly progressive *a*- and *b* wave amplitude reduction was recorded together with (2) a progressive increase of the latencies of the oscillations. The *b* wave peak latency (3) in this phase first decreased but later was normalized and sometimes even increased a little. These slow changes probably are due to the prolonged slow dissociation of iron ions in connection with the capsule resorption.

The initial phase was studied more closely by injecting an iron salt solution into the vitreous. The resulting ERG findings were similar to those recorded in the initial phase and in addition an amplitude reduction of the oscillatory potential was found. After an hour the oscillations were hardly discernible.

As mentioned in the introduction the ERG following the intraocular implantation of iron pieces has been studied in the rabbit. *Sugita et al* (1960) inserted iron pins (8×1 mm) and *Seto* (1960) iron particles 3×0.75 mm into the vitreous. The resulting ERG changes were followed for a short time only, one and two months respectively. *Sugita et al* reported that the *b*-wave of the ERG either increased, was normal or decreased. *Seto* on the other hand found that the *b*- and *c*-waves decreased day by day. In both works a trend of the *b*-wave latency to increase was reported. The initial changes found in the pre-

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As pointed out the present results indicate two phases in the development of siderotical changes in the retina. The initial phase is probably related to the sudden exposure to the retina of a heavy dose of metal ions immediately after the implantation of the particles and is characterized by the following ERG findings: (1) a partly reversible reduction of the *a*- and *b*-wave amplitudes, (2) a normal or even a slightly increased *b* wave peak latency and (3) a slight or moderate increase of the latencies of the oscillations of the oscillatory potential. In the second phase (1) a slowly progressive *a*- and *b*-wave amplitude reduction was recorded together with (2) a progressive increase of the latencies of the oscillations. The *b*-wave peak latency (3) in this phase first decreased but later was normalized and sometimes even increased a little. These slow changes probably are due to the prolonged slow dissociation of iron ions in connection with the capsule resorption.

The initial phase was studied more closely by injecting an iron salt solution into the vitreous. The resulting ERG findings were similar to those recorded in the initial phase and in addition an amplitude reduction of the oscillatory potential was found. After an hour the oscillations were hardly discernible.

As mentioned in the introduction the ERG following the intraocular implantation of iron pieces has been studied in the rabbit. Sugita *et al* (1960) inserted iron pins (8×1 mm) and Seto (1960) iron particles 3×0.75 mm into the vitreous. The resulting ERG changes were followed for a short time only, one and two months respectively. Sugita *et al* reported that the *b* wave of the ERG either increased, was normal or decreased. Seto on the other hand found that the *b*- and *c*-waves decreased day by day. In both works a trend of the *b*-wave latency to increase was reported. The initial changes found in the pre-

upon the size of the metal area, the particles reappeared. About half a year of a year later however a new thinner capsule slowly developed.

A temporal correlation between the ERG changes and the capsule formation and resorption was demonstrated. During the first days after the implantation the following changes were recorded: (1) a reversible a and b wave amplitude reduction, (2) a normal or a slightly increased peak latency of the scotopic b wave and (3) a moderate increase of the peak latencies of the oscillations of the oscillatory potential. These changes probably are to be ascribed to a retinal oedema as a result of the sudden exposure of a heavy dose of iron ions dissociated from the metal just after the implantation. By injecting an iron chloride solution into the vitreous a similar condition, i.e. a retinal oedema was obtained. In addition to the changes accounted for above an obvious amplitude reduction of the oscillatory potential was recorded.

In connection with the reappearance of the iron particles slow progressive ERG changes were recorded: (1) an a and b wave amplitude reduction and (2) a marked increase of the peak latencies of the oscillations. The b wave peak latency (3) first decreased but later was normalized and sometimes even increased a little. A reduction of the amplitude of the oscillatory potential was found to occur. This reduction however was not more pronounced than that of the b wave. In the final recordings before the potentials disappeared these oscillations even dominated the records.

References

- Algere P (1963) Clinical studies on the oscillatory potentials of the human electroretinogram with special reference to the scotopic b wave. *Acta ophthalm.* 46: 935.
- Algere P, Hedin A & Kock E (1963) The electroretinogram and histopathology in experimental uveitis of the pigeon. *Acta ophthalm.* 46: 970.
- Arden G B & Brown K T (1965) Some properties of components of the cat ERG revealed by focal recording under oil. *J. Physiol.* 116: 479.
- Atlas and textbook of ophthalmic pathology (1957) W B Saunders Company Philadelphia London p 169.
- Bornschein H & Zwiener A (1952) Das Elektroretinogramm des Kaninchens bei experimenteller Erhöhung des intraokularen Druckes von Graefes *Arch. Ophthalm.* 15: 527.
- Brown K T (1964) The electroretinogram: its components and their origins. *Vision Res.* 8: 633.
- Brown K T, Watanabe K & Murakami M (1965) The early and late receptor potentials of monkey cones and rods. Cold Spring Harbor Symp. Quant. Biol. 30: 457.
- Brown K T & Wiesel T N (1961a) Analysis of the intraretinal ERG in the intact cat eye. *J. Physiol.* 153: 29.
- Brown K T & Wiesel T N (1961b) Localization of origins of ERG components by intraretinal recordings in the intact cat eye. *J. Physiol.* 158: 257.

tion with a retinal oedema and/or a posterior uveitis has been reported in man (Yonemura *et al* 1962) and in pigeon (Algvere *et al* 1968). Although not directly supporting the abovementioned theory a similar increase of the *b* wave peak latency in connection with a corresponding amplitude reduction has been reported after thrombosis of the central retinal vein in man (Müller & Haase 1968) and after raising the intraocular pressure in the rabbit eye (Bornschein & Zwiauer 1952).

In intraretinal microelectrode experiments (see *e.g.* Brown 1968) the maximal amplitudes of the oscillatory potential were found in the inner nuclear and outer plexiform layers and the oscillations were considered to be generated from reverberating circuits in the feed back mechanisms of the retinal neuronal network. This concept on the origin of the oscillatory potential might well agree with the findings of the present work *viz.* reduced oscillations in eyes with a retinal oedema and preserved oscillations in eyes with a slowly progressive retinal atrophy due to siderosis. In retinal oedema the intercellular space will expand and the cells will be pushed away from each other causing a deterioration of the intercellular connections. Thus the basic mechanisms of the oscillatory potential are damaged and the oscillations will be less pronounced. The atrophy in retinal siderosis mainly involves the peripheral parts of the retina (see Duke-Elder 1954) the central parts being left preserved. The ERG potentials generated from this preserved central field probably are shunted by the degenerated tissue of the peripheral retina and will thus be diminished at the active electrode on the cornea (Harpe 1948). It is to be expected that the oscillatory potential will be reduced in the same way and by the same order of magnitude as the *B* or *b* wave. This is what was found in the present study.

However Yonemura *et al* (1962) reported that the oscillatory potential usually "disappeared" in *siderosis retinae* and Algvere (1968) found "extinguished" oscillations in one case of siderosis. In two additional cases "modified" oscillations were reported (Perdriel *et al* 1964). Many factors may be responsible for the differences between these results and those of the present study *e.g.* extent and type of siderotic damage, difference in recording techniques etc.

Summary

The ERG and ophthalmological changes following the implantation of pure iron particles in the vitreous were studied in long term experiments in the rabbit.

The particles were encapsulated soon after the implantation. After about a week the capsule began to resorb and after a varying period of time depending

upon the size of the metal area the particles reappeared. About half a year of a year later however a new thinner capsule slowly developed.

A temporal correlation between the ERG changes and the capsule formation and resorption was demonstrated. During the first days after the implantation the following changes were recorded: (1) a reversible *a* and *b* wave amplitude reduction, (2) a normal or a slightly increased peak latency of the scotopic *b*-wave and (3) a moderate increase of the peak latencies of the oscillations of the oscillatory potential. These changes probably are to be ascribed to a retinal oedema as a result of the sudden exposure of a heavy dose of iron ions dissociated from the metal just after the implantation. By injecting an iron chloride solution into the vitreous a similar condition with a retinal oedema was obtained. In addition to the changes accounted for above an obvious amplitude reduction of the oscillatory potential was recorded.

In connection with the reappearance of the iron particles slow progressive ERG changes were recorded: (1) an *a* and *b* wave amplitude reduction and (2) a marked increase of the peak latencies of the oscillations. The *b* wave peak latency (3) first decreased but later was normalized and sometimes even increased a little. A reduction of the amplitude of the oscillatory potential was found to occur. This reduction however was not more pronounced than that of the *b* wave. In the final recordings before the potentials disappeared these oscillations even dominated the records.

References

- Aligvere P (1963) Clinical studies on the oscillatory potentials of the human electroretinogram with special reference to the scotopic *b* wave. *Acta ophth* 46: 933.
- Aligvere P, Hedén A & Lock E (1968) The electroretinogram and histopathology in experimental uveitis of the pigeon. *Acta ophth* 46: 920.
- Arden G B & Brown A T (1965) Some properties of components of the cat ERG revealed by focal recording under oil. *J Physiol* 116: 429.
- Atlas and textbook of ophthalmic pathology (1957) W B Saunders Company Philadelphia London p 169.
- Bornheim H & Fawcett A (1952) Das Elektoretinogramm des Kaninchens bei experimenteller Erhöhung des intraokularen Druckes von Graefes *Arch Ophth* 152: 577.
- Brown A T (1964) The electroretinogram: its components and their origins. *Vision Res* 4: 633.
- Brown A T, Watanabe K & Murakami M (1965) The early and late receptor potentials of monkey cones and rods. C 1d Spring Harbor Symp Quant Biol 30: 457.
- Brown K T & Wiesel T N (1961a) Analysis of the intraretinal ERG in the intact cat eye. *J Physiol* 118: 779.
- Brown K T & Wiesel T N (1961b) Localization of origins of ERG components by intraretinal recordings in the intact cat eye. *J Physiol* 118: 257.

- Detwiler S R* (1943) *Vertebrate photoreceptors* The Mac Millan Company New York p 19
- Duke Elder S* (1954) *Textbook of Ophthalmology* Henry Kimpton London 6 61/3
- Granit R* (1932/33) The components of retinal action potential in mammals and their relation to the discharge in the optic nerve *J Physiol* 77 207
- Granit R* (1935) Two types of retinæ and their electrical responses to intermittent stimuli in light and dark adaptation *J Physiol* 85 421
- Granit R* (1947) *Sensory mechanisms of the retina* Oxford University Press London
- Granit R* (1955) *Receptors and sensory perception* Yale University Press New Haven
- Karpe G* (1948) Early diagnosis of siderosis retinæ by the use of electroretinography *Docum ophth* 2 277
- Karpe G* (1957) Das Elektoretinogramm bei Siderosis bulbi *Bibl Ophth* 48 187
- Knave B* (1969a) Electroretinography in eyes with retained intraocular metallic foreign bodies. A clinical study *Acta ophth Suppl* 100
- Knave B* (1969b) Long term effects of high intensity flashes on the ERG of the rabbit (In preparation for *Acta physiol scandinav*)
- Knave B* (1969c) Long term changes in retinal function induced by short, high intensity flashes *Experientia* 25 319
- Knave B* (1969d) The ERG and ophthalmological changes in experimental metallosis in the rabbit II Effects of steel copper and aluminium particles (In preparation for *Acta Ophth*)
- Knave B & Koch E* (1969) Structural and functional changes in metallosis bulbi (Unpublished observations)
- Kolker A E, Moses R A, Constant M A & Becker B* (1963) The development of glaucoma in rabbits *Invest Ophth* 2 316
- Kousssek V* (1965) Electroretinographie et Microscopie Electronique dans les Metalloses *Ann ocul* 198 694
- Leber Th* (1891) *Die Entstehung der Entzündung* Verlag Wilhelm Engelmann Leipzig
- Müller W & Haase E* (1968) Measuring of peak times in patients with thrombosis of the vena centralis retinæ *Advances in electrophysiology and - pathology of the visual system Proc of the 6th ISCLERG Symp VFB Georg Thieme Leipzig* p 351
- Noell W K* (1954) The origin of the electroretinogram *Am J Ophth* 38 78
- Perdriel G, Soussens G, Desbordes P & Leblanc M* (1964) Physiopathologie des ondes «E» de l'électroretinogramme *Bull Mem Soc Franç Ophthal* 77 77
- Schmoger F* (1956) Elektoretinographie bei Siderosis und Chalcosis *Klin Monatsbl Augenhe* 128 158
- Seto Y* (1960) The influence of intraocular iron pieces on the electroretinogram (ERG) *Acta Soc Ophth Jap* 64 1420
- Straub W* (1961) *Das Elektoretinogramm* Bucherei des Augenarztes Ferdinand Enke Verlag Stuttgart
- Sugita Y, Yodohawa M & Tanabe T* (1960) Electroretinographic studies in experimental siderosis *Acta Soc Ophth Jap* 64 1427
- Yonemura D, Tsunuki H & Aoki T* (1962) Clinical importance of the oscillatory potential in the human ERG *Acta ophth Suppl* 70 115
- Yonemura D, Masuda Y & Hattai M* (1963) The oscillatory potential in the electroretinogram *Jap J Physiol* 13 129

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THE ERG AND OPHTHALMOLOGICAL CHANGES IN EXPERIMENTAL METALLOSIS IN THE RABBIT

II Effects of steel copper and aluminium particles

BY

BENGT KNAVE

Introduction

Retained intraocular metal particles can give rise to tissue damage in the different parts of the eye called *metallosis bulbi*. Retinal damage occurs at an early stage and is the most detrimental results of metallosis. This damage has been studied by means of ERG in clinical works (Karpe 1948, 1957, Schmoger 1956, Straub 1961, Housch 1965, Knave 1969a).

In the clinical investigation by Knave (1969a) the results indicated that minor differences in the alloy content of steel particles might be important for the occurrence of siderosis bulbi. This has been studied more closely in the rabbit in the present work which also can be regarded as a complement to a recent investigation on the long term effects following the implantation of pure iron particles into the rabbit vitreous (Knave 1969b). Moreover the ERG following the intravitreal implantation of copper and aluminium particles has also been studied in the present work since this has not been done before and since particles of copper and aluminium next to those of iron and steel are the most commonly occurring intraocular metal foreign bodies in the human eye.

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Material and Methods

The ERG method as well as the ophthalmological examination and implantation techniques have been described elsewhere (Knaue 1969b, c)

The composition of the implanted steel particles (Sandvik) is presented in Table I

The different alloys were chosen for various reasons. In the clinical study by the author (Knaue 1969a) the particle size and location were almost identical in two cases. In one of these cases there were no signs of siderosis 10 months after the accident when the particles entered the eye. In the other case advanced siderotical changes appeared after only 5 months. The main difference between these cases was the alloy content of the particles. In the first mentioned case the particle contained 5% nickel. In the second mentioned only 1%. Because of this difference 2XN5 steel particles were implanted in order to be able to compare the resulting changes with those reported in another study where pure iron particles were implanted (Knaue 1969b). The 6R60, 6C27 and HT2 steels are stainless with a varying degree of corrosion resistance. The 6R60 steel is highly corrosion resistant. All the steels presented in Table I as well as the corrosive carbon steels i.e. iron alloyed with minor quantities of carbon are used in different tools depending upon their specific properties.

The implanted copper particles (Mallinckrodt) had a copper content of 99.8 per cent and the aluminium particles (KEBO) an aluminium content of 99.97 per cent.

All the implanted particles were cubes with a side of 0.4-0.5 mm. This was also the case with the pure iron particles the implantation of which was described in another work (Knaue 1969b).

The present study reports the results of long term experiments in which steel, copper and aluminium particles were implanted in the vitreous of the right eyes of seven rabbits. Four rabbits received 15 steel particles each, one received 15 aluminium particles. The number of 15 was chosen in order to be

Table I
The composition (in per cent) of the implanted steel particles

Steel	Cr	Ni	Mo	Si	Mn	C	Fe
2XN5		5.2		0.1	0.4	0.1	94.0
HT2	5.0			1.9	0.2	0.1	92.8
6C27	14.0			0.2	0.3	0.3	85.2
6R60	17.8	12.3	2.8	0.6	1.5		64.1

able to compare the present results with those reported in another study where 15 particles of pure iron were implanted (Knaue 1969b). When implanting copper particles however the vitreous reaction was found to be intense enough following the implantation of 8 particles and in the seventh animal therefore only 4 copper particles were implanted. In all experimental series the left eye served as normal reference (see Knaue 1969b).

Results

Implantation of differently alloyed steel particles

a) 0.5% Ni steel. In one of the experiments 15 steel particles (2NX5) containing 0.5% nickel were implanted. The ERG results of this experiment are presented in Fig. 1. Fig. 1A shows the resulting changes in amplitudes (filled circles) and the scotopic *b* wave peak latency (squares) expressed in per cent of the values for the intact fellow eye. The *a* wave amplitude is represented by a solid line, the *b* wave by a dotted line and the *B* wave (measured from the peak of the *a* wave to the peak of the *b* wave) by a broken line. Fig. 1B shows the peak latencies of the first five positive oscillations of the oscillatory potential (triangles o_1 , o_2 , o_3 , o_4 and o). When affected these latencies always were found to increase. This increase is expressed in msec compared to the latencies of the intact fellow eye.

As can be seen in Fig. 1A the amplitudes of the potentials rapidly decreased after the implantation. After a couple of days however they increased to a subnormal level of about 50-60 per cent between the 25th and 60th day. During the following 4 months a slow reduction occurred. From about the 190th day the amplitudes were found to be subnormal at the 20 per cent level.

The scotopic *b* wave peak latency did not change until 18 days after the implantation when subnormal values were recorded. After 25 days the latency was found to be 10 per cent of that of the intact fellow eye. From then on however the latency started to increase and reached normal values after 150 days.

The latencies of the oscillatory potential were moderately increased during the first 30-40 days. During the following month a slight trend towards normal values was noted but this trend was interrupted by a new very slow increase from the 60th day. The amplitude of the oscillations diminished concurrently with the *b* wave amplitude and by the same order of magnitude.

Ophthalmological examination showed that there were insignificant changes in the anterior segment. An aqueous flare was noted during the first week after implantation. A slight pigment granulation on the anterior lens capsule was

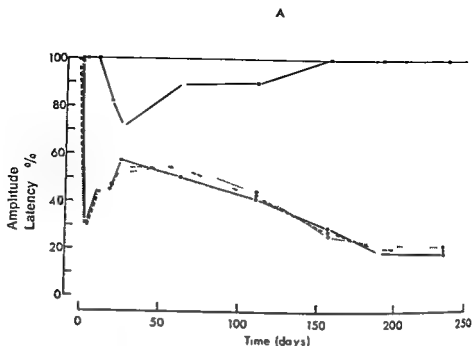


Fig 1 A

Amplitudes (filled circles) of *a* wave (solid line) *B* wave (broken line) and *b* wave (dotted line) and *b* wave peak latency (squares) of the ERG following the intravitreal implantation of 15 steel particles alloyed with 5% Ni. Implantation performed at zero on horizontal time axis

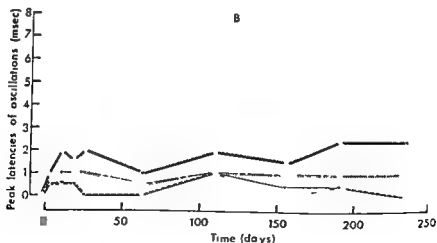


Fig 1 B

Peak latencies of the five first positive oscillations of the oscillatory potential (o_1 thin solid line o_2 broken line o_3 dotted line o_4 dotted broken line o_5 heavy solid line) of the ERG in the experiment described in Fig 1 A

seen in the corneal microscope as the only pathological finding of the anterior segment throughout the rest of the observation period

Special interest was paid to the reaction of the vitreous substance to the implanted particles. A day or two after the implantation a capsule was formed around the particles. This capsule was white and diffusely delimited and was maximal at about the 10th day. From then on a slow progressive resorption of the capsule occurred. About 60 days after the implantation most of the particles were seen as glistening metal. After about 160 days a new encapsulation process was detected, this second capsule being much thinner than the first one persisted throughout the rest of the observation period.

At the same time as the initial capsule was formed small white wads were seen in the vitreous. Most of these wads were later resorbed. Some of them though persisted and were located preretinally which gave rise to local retinal atrophies seen toward the end of the experiment. It should also be mentioned that remains of the initial capsule persisted forming the main parts of strands extending through the vitreous. Moreover at direct ophthalmoscopy a glistening reflex from the peripheral parts of the fundus could be seen from about the 30th day. This glistening reflex persisted until the end of the experiment.

In this experiment there was a temporal correlation between the ERG changes and the capsule formation and resorption in the same way as was shown photographically in experiments in which pure iron particles were implanted (Anave 1969b). Thus for the 5% Ni steel one may conclude that just after the implantation the retina is exposed to a sudden and heavy dose of toxic iron ions which results in a decrease of the ERG. This decrease is reversible and is assumed to be due to a diminishing ion dissociation following the encapsulation of the particles. When the particles are slowly decapsulated the ERG again decreases. At the end of the experiment a new capsule develops which probably accounts for the constant amplitudes recorded during the last 45 days. In the above mentioned study (Anave 1969b) the initial reversible ERG changes were suggested to represent a retinal oedema while the later progressive ERG changes were assumed to be due to a retinal atrophy.

b) 5% Cr steel In this experiment 15 steel particles (HT2) containing 5% chromium were implanted. The resulting ERG changes are shown in Fig. 2A. No latency data are presented because they did not differ from those recorded in the intact fellow eye. As can be seen in the diagram an initial reversible reduction was recorded during the first 10 days the b wave being more reduced than the a wave. From then on during the rest of the experimental period the a wave was found normal. The H and B waves were found slightly increased between the 10th and 180th day. From then on they decreased and reached subnormal values after 300 days. This decrease was slightly more pronounced 400 days after the implantation.

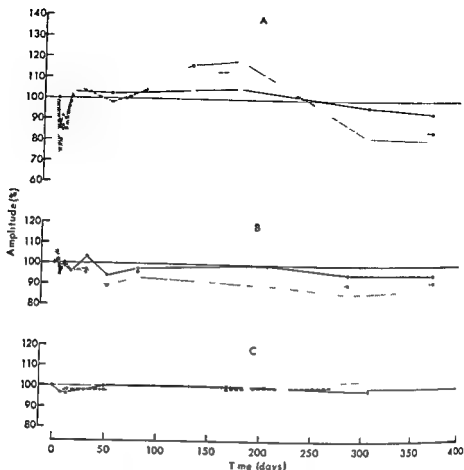


Fig 2

Amplitudes of *a* wave (solid line) *B* wave (broken line) and *b* wave (dotted line) of the ERG following the intravitreal implantation of 15 steel particles alloyed with 5% Cr (A) 14% Cr (B) and 18% Cr 12% Ni 3% Mo (C) Implantation performed at zero on horizontal time axis

The reaction of the vitreous substance to the implanted particles in this experiment differed from that of the preceding one. After about 10 days a thin white yellow coating was seen to cover parts of the particles. This coating very slowly diminished and after about 130 days most of the particles were seen uncovered in a condition that remained constant during the remaining observation period. It should be mentioned that a few preretinal wads were noted between the 100th and 200th day after which time they could not be detected. Moreover, in contrast to the experiments where iron or 5% Ni steel particles were implanted, no glistening reflex was seen.

c) 14% Cr steel In this experiment 15 steel particles (6C27) containing 14% chromium were implanted. The resulting ERG changes are shown in Fig. 2B. Like the experiment where 5% Cr steel particles were implanted, no latency data are presented because they did not differ from those of the intact fellow eye. As can be seen in the diagram, the resulting changes of the amplitudes are within normal limits (see Knave 1969b), although the *b* wave constantly was recorded somewhat more reduced than the *a* wave.

Ophthalmoscopically the particles were seen glistening and quite uncovered up to the last observation, when a very thin white coating partly covered some of the particles. A couple of very small wads were seen in the vitreous between the 100th and 200th day, but not later. After the 200th day a very slight glistening fundus reflex was seen in the lower parts of the fundus.

d) 18% Cr 12% Ni 3% Mo steel In one eye 15 particles of this highly corrosion resistant steel (6R60) were implanted. Fig. 2C shows that the ERG potentials of this eye did not differ from those of the intact fellow eye. Ophthalmoscopically a thin coating, partly covering some of the particles, was detected at about the 150th day. This coating was found to be increased after 300 days. No glistening fundus reflex or vitreal wads were noted in this experiment.

Implantation of aluminium particles

In one experiment 15 aluminium particles were implanted. The resulting ERG changes are shown in Fig. 3. As can be seen in Fig. 3A, the amplitudes first decreased temporarily. The *a* wave was then found to increase between the 10th and 20th day, normal values being reached 40 days after the implantation. The *b* and *B* waves were subnormal the first 20 days and on the 40th day normal values were again recorded. From the 40th day on, the amplitudes diminished slowly. There was a conspicuous difference between the reduction of the *a* wave and that of the *b* and *B* waves, the latter ones being considerably more reduced. At the end of the experiment the *B* wave approached zero, while the amplitude of the *a* wave still remained at about 90 per cent of the amplitude of the intact fellow eye.

Following an initial reversible increase, the peak latency of the *b* wave was found to increase slowly after the 140th day. As seen in Fig. 3B, the latencies of the oscillatory potential were also found to increase slowly after the 140th day. The amplitude of the oscillatory potential was found to be reduced to the same extent as the reduction of the *B* wave.

Ophthalmologically only insignificant changes occurred. The particles were seen uncovered except during the last months of the experiment, when a thin white coating developed, covering parts of some of the particles.

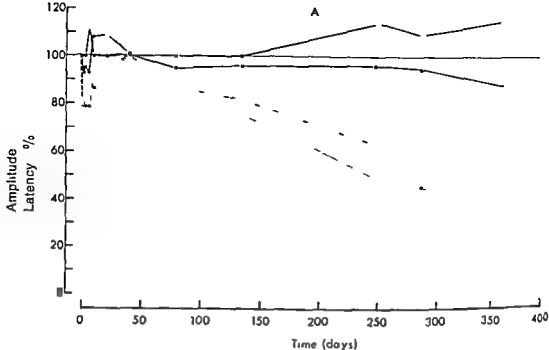


Fig 3A

Amplitudes (filled circles) of *a* wave (solid line) *B* wave (broken line) and *b* wave (dotted line) and *b* wave peak latency (squares) of the ERG following the intravitreal implantation of 15 aluminium particles. Implantation performed at zero on horizontal time axis

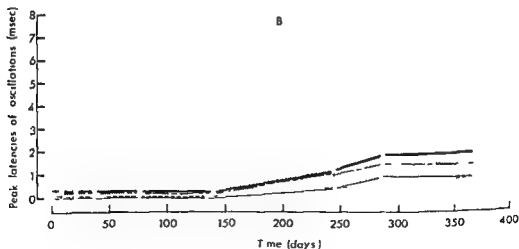


Fig 3B

Peak latencies of the five first positive oscillations of the oscillatory potential (o_1 thin solid line o_2 broken line o_3 dotted line o_4 dotted broken line o_5 heavy solid line) of the ERG in the experiment described in Fig 3A

Implantation of copper particles

a) Implantation of 8 copper particles In this experiment only 8 particles were implanted since copper is known to be very toxic to the tissues of the eye (see *Knave 1969a*). The resulting ERG changes are presented in Fig. 4. The *a*- and *b* wave amplitudes (Fig. 4A) rapidly decreased during the first three days after implantation. During the following two weeks the decrease continued but at a considerably slower rate. Between the 15th and 35th day more or less constant subnormal amplitudes were recorded at a level between 25 and 40 per cent. It should also be mentioned that throughout this experiment the *a* wave was found to be less reduced than the *M* and *b* waves. From the 35th day a new reduction occurred until the 57th day when no potentials could be recorded.

The *b* wave peak latency first increased slightly. After a couple of days a decrease to subnormal values occurred. This decrease was slowly reversible; normal values were reached at the end of the experiment.

The latencies of the oscillations of the oscillatory potential (Fig. 4B) did not change during the first five days but during the following ten days an increase was noted. During the remaining experimental period there was again a low increase. The amplitudes of the oscillations were reduced by the same order of magnitude as the *B* and *b* waves.

An aqueous flare was visible during the first two weeks. Pigmented granules on the anterior lens capsule, however, could be seen from the first day after the implantation to the last day of observation.

A dense thick yellowish white capsule was formed around each particle. Some of the particles located peripherally were fully encapsulated after a few days. The encapsulation of particles located centrally in the vitreous was slower and was not completed until two weeks after the implantation.

One day after the implantation a diffuse white blue opacity was discernible as a thin veil in large parts of the vitreous. This diffuse opacity changed after some days; it became more white and delimited and after about two weeks it was divided into parts, some of which formed strands extending through the vitreous. After the same time, i.e. after about two weeks, a glistening reflex from the fundus could be seen at direct ophthalmoscopy. This pathological reflex persisted to the end of the experiment.

The capsules around each copper particle appeared as yellowish white halos in the vitreous. After a month some of these capsules were seen ruptured with capsule material spread in the vitreous. At least one copper particle was seen partly decapsulated with the metal glistening. During the last weeks the vitreal opacities successively increased and a posterior cortical cataract was also seen at the end of the experiment.

There is a temporal correlation between the electroretinographical and ophthalmological changes. The initial capsule formation may thus account for the

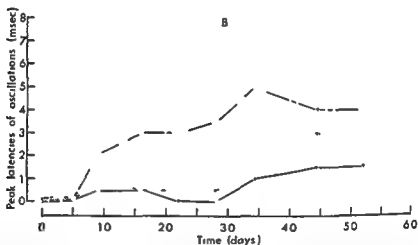
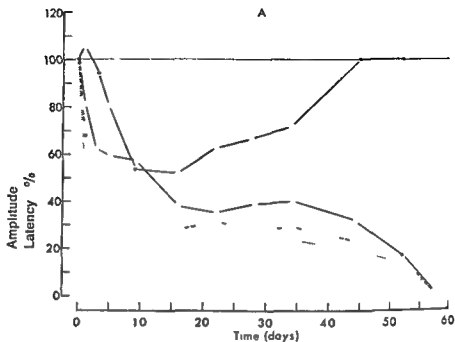


Fig 4A

Amplitudes (filled circles) of *a* wave (solid line) *B* wave (broken line) and *b* wave (dotted line) and *b* wave peak latency (squares) of the ERG following the intravitreal implantation of 8 copper particles. Implantation performed at zero on horizontal time axis

Fig 4B

Peak latencies of the five first positive oscillations of the oscillatory potential (*o*₁ thin solid line *o*₂ broken line *o*₃ dotted line *o*₄ dotted broken line *o*₅ heavy solid line) of the ERG in the experiment described in Fig 4A

interruption at the 10th day of the initial ERG decrease. The rupture of the capsules seen at the 30th day with the subsequent deterioration of vitreal structure probably accounts for the final ERG reduction.

b) Implantation of 4 copper particles Because of the intense reaction in the eye after the implantation of 8 copper particles only 4 particles were implanted in this experiment. Fig. 5 shows the resulting ERG changes. No latency data are presented because they did not differ from those of the intact fellow eye. As can be seen in the diagram a sudden increase was recorded after about 10 days. This increase was reversible, normal values being reached after about 100 days. From then on however a new reversible increase was recorded. This time the normal values were not reached until 200 days later, i.e. 300 days after the implantation. During the remaining experiment period normal values were obtained. When the ERG was found increased the *b* and *B* waves always were more increased than the *a* wave.

On ophthalmological examination the particles were found encapsulated a few days after the implantation. The diffuse white blue opacity seen as a thin veil in the vitreous in the preceding experiment was also seen in this experiment. However it was only seen in a narrow sector surrounding all the particles and it disappeared after three weeks.

Very small and highly glistening particles were seen in the vitreous 300 days

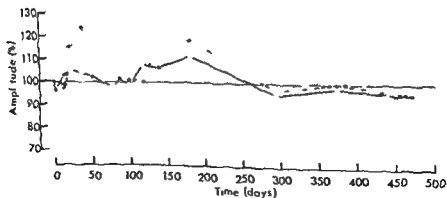


Fig. 5
Amplitudes of *a* wave (solid line) *B* wave (broken line) and *b* wave (dotted line) of the ERG following the intravitreal implantation of 4 copper particles. Implantation performed at zero on horizontal time axis.

after the implantation. The glistening particles increased in number during the remaining experiment period.

The capsules seen as yellowish white balls in the vitreous changed the colour toward yellow after 300 days. Moreover, after 400 days one of the capsules was seen clearly diminished so that the contours of the particle were visible.

Discussion

The general course of ERG changes as well as the ophthalmological changes following the implantation of steel particles alloyed with 5% Ni were similar to the changes after the implantation of pure iron particles (Knave 1969b) and the results indicate an initial reversible oedema followed by a progressive atrophy of the retina. After the implantation of pure iron particles the ERG was non recordable after 100 days. This detrimental course, however, did not occur in the 5% Ni experiment. After 100 days the ERG amplitudes were still 45% of those obtained in the intact fellow eye and after 230 days a 20% response remained. These results thus confirm the clinical study (Knave 1969a) viz. that even minor differences in the alloy content of the steel particles may influence the development of *siderosis bulbi*.

The implantation of steel particles alloyed with 5% Cr resulted in electroretinographical and ophthalmological changes entirely different from those recorded after the implantation of pure iron particles and particles alloyed with 5% Ni. Initially a thin coating covered the particles. This coating diminished and after about 130 days most of the particles were seen uncovered. At this time and some months later a slight increase of the *b* wave was recorded. An increased ERG response was also recorded after the implantation of 4 copper particles. In that experiment all the potentials were increased, the *b* wave, however, more than the *a*-wave.

It should be mentioned that in some of the clinical studies an increase of the ERG response has been described (see e.g. Karpe 1957 and Knave 1969a) as an early manifestation of *metallois bulbi*. The increased ERG potentials recorded in the present work (Fig. 2A and Fig. 5) probably represent an early manifestation of retinal metallosis too.

The implantation of corrosion resistant steel particles (14% Cr and 18% Cr 12% Ni 3% Mo) did not induce any significant changes. There was only a very slight reduction of the ERG in the 14% Cr experiment and no changes in the ERG were noted in the other experiment. The conclusion is that the dif

ference following the implantation of iron and steel particles depends on a lower iron ion dissociation rate of the steel particles. The development of a slight coating on some of these particles and the appearance of a pathological glistening reflex from the fundus at ophthalmoscopy are in agreement with the view stated by *Duke Elder* (1954) that inert foreign bodies cannot be regarded as harmless to the eye.

In the clinical study by the author (*Knave* 1969a) most of the eyes with retinal metallosis showed a *b* wave reduction that was more pronounced than that of the *a* wave. In some eyes however the *a* and *b* waves were equally reduced. Therefore the experiment in which 15 aluminium particles were implanted is of special interest since in this experiment the *b* wave was considerably more reduced than the *a* wave. A similar tendency was also noted in the above mentioned steel experiments where particles alloyed with 5 and 14 % Cr were implanted. In the experiments where particles of pure iron and particles alloyed with 5 % Ni were implanted this difference did not exist. These findings indicate that the retinal exposure to a heavy dose of toxic metal ions results in an ERG where the *a* and *b* wave are equally reduced. A probable explanation is that the *a* and *b* wave generating structures are reached at about the same time by the toxic metal ions. The finding that a prolonged exposure to a moderate dose of ions results in ERGs in which the *b* wave is more reduced may depend on the fact that the ions reach the structures that generate the *b* wave before they reach those generating the *a* wave (see *Knave* 1969b). This may also explain why the *b* wave was found more reduced than the *a* wave in the 8 copper particle experiment.

Intraocular copper particles are known to give rise to a rapidly developing detrimental eye damage (see e.g. *Duke Elder* 1954). This also occurred in the present study after implanting 8 copper particles in the vitreous of a rabbit eye. The resulting ERG and ophthalmological changes indicated the existence of two phases in the development of the retinal damage: (1) an initial phase which may be due to an oedema and (2) a later one which is assumed to be due to a slowly developing retinal atrophy.

As mentioned above the implantation of 4 copper particles was followed by a long lasting increase of the ERG (especially of the *b* wave). This super-normal ERG may be the first and only sign of retinal metallosis in this case. *Straub* (1961) after implanting a brass particle in the anterior chamber in two rabbit eyes also found the *b* wave to be reversibly increased.

According to *Duke Elder* (1954) highly brilliant deposits in the fundus represent one of the characteristic reactions to retained intraocular copper particles. In the 4 copper particle experiment a similar finding was noted: very small highly glistening particles were seen in the vitreous 300 days after the implantation. Because of their small size it was not possible to estimate their nature.

Summary

In the present work the ERG and ophthalmological changes were studied following the implantation of steel aluminium and copper particles in the vitreous of the rabbit eye

Minor differences in the alloy content of the implanted steel particles were shown to play an important role in the development of *siderosis bulbi*. The results after implantation of steel particles alloyed with 5 per cent nickel resembled those obtained in another study where pure iron particles were implanted (Anave 1969b)

In three rabbits steel particles alloyed with (1) 5% Cr (2) 14% Cr and (3) 18% Cr-12% Ni 3% Mo were implanted. In the first mentioned of these experiments a long lasting reversible increase of the ERG was recorded the *b* wave being more increased than the *a* wave. This increase was followed by a slight decrease the *b*-wave being more reduced than the *a*-wave. In the second mentioned experiment a slowly developing small reduction of the ERG was observed also here the *b*-wave was more reduced than the *a* wave. In the third-mentioned experiment normal ERGs were recorded.

The encapsulation reactions to these three alloys also differed from those observed after implantation of pure iron particles. Only a thin coating developed covering parts of the particles. In the second- and third mentioned experiments this coating was noted as late as 10-14 months after the implantation.

The implantation of aluminium particles resulted in a slow reduction of the *b*-wave so that after about 300 days practically no *b* wave was obtained. The *a*-wave on the other hand was only reduced to 90 per cent. Only slight ophthalmological changes were noted e.g. a partial thin coating of some of the particles at the end of the experiment.

In two eyes copper particles were implanted. The toxicity of copper ions resulted in a rapidly developing vitreal damage and deterioration of the ERG. The implantation of a reduced number of particles resulted in an increased ERG response recorded for long periods and interpreted as an early manifestation of retinal metallosis.

References

- Duke Elder S (1954) Textbook of Ophthalmology Henry Kimpton London 6 6173
Karpe G (1948) Early diagnosis of siderosis retinae by use of electroretinography
Docum Ophth 2 277
Karpe G (1957) Das Elektretinogramm bei Siderosis bulbi Bibl Ophth 48 182

- Knave B* (1969a) Electoretinography in eyes with retained intraocular metallic foreign bodies. A clinical study. *Acta Ophth Suppl* 100
- Knave B* (1969b) The ERG and ophthalmological changes in experimental metallosis in the rabbit. I. Effects of iron particles. (In preparation for *Acta Ophth*)
- Knave B* (1969c) Long term effects of high intensity flashes on the ERG of the rabbit. (In preparation for *Acta physiol scand*)
- Loouck V* (1965) Electoretinographie et Microscopie Electronique dans les Metalloses. *Ann Ocul* 198: 694
- Schmoger E* (1956) Elektoretinographie bei Siderosis und Chalcosis. *Klin Monatsbl Augenh* 103: 153
- Straub W* (1961) Das Elektoretinogramm. *Bucherei des Augenarztes Ferdinand Enke Verlag* Stuttgart

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Report of the Norwegian Ophthalmological Society's Annual Meeting November 1968

Weidemann J *Loues Occulocerebral syndrome*

One year ago the author reported a similar case a boy who later died. The mother remarried and now has a girl with the same disease. There was microphthalmus on the left side and cataract on both sides. There were also signs of kidney and brain damage. Chromosomal testing showed female. It is usually always boys who are affected by this disease.

Hvidsten Hanne *Cortisone treatment of malignant exophthalmos - a case report*

Eleven patients were reported with exophthalmos treated with large doses of steroids. Seven patients showed considerable improvement during the first weeks. The subjective complaints particularly were reduced. However recession measured with the exophthalmometer was more uncertain.

Discussion *Waaen* asked whether anyone had experience with ismelin. *Ytterbor* replied that ismelin might be of some help on the retraction of the eyelids but scarcely on the exophthalmos itself. Many patients felt that the drops burned unpleasantly. *Roe* and *Maartmann Moe* mentioned the strongly swinging tension values frequently found in exophthalmic eyes that were almost certainly due to technical difficulties with the tonometry. *Thomassen* mentioned the difficulties of judging the results of the treatment of malignant exophthalmos since the degree of exophthalmos follows a rising curve spontaneously sinking. He said that by the use of large doses of corticosteroids he really had the feeling for the first time that the treatment was effective. *Horter*: Some patients with malignant exophthalmos first come for treatment when they have large corneal ulcers and cortisone treatment is then questionable. The question is then whether pressure relieving operation like the Kronlein's operation is indicated. *Beitel sen* had never seen such a serious case that had really indicated such a drastic operation.

Haugen H N *Cortisone treatment of exophthalmos*

First the two types of exophthalmos were mentioned i.e. the non infiltrative benign and the infiltrative malignant. In the latter case it is not an excess of thyroid stimulat

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ing hormone but pathological amounts of long acting thyroid stimulator (LATS) and exophthalmos producing substance. The treatment of this latter group of patients has so far been very unsatisfactory. However large doses of corticosteroids seem to be effective. Initial doses of 100-120 mg Prednisolon are recommended.

The doses are reduced as quickly as possible. The treatment gives not only a subjective effect because the concentration of LATS is considerably reduced. Some cases need a continuing dose of 10-12 mg Prednisolon over a long period. A discussion followed on the indications for operative treatment by the method of Kronlein or Naftziger.

The diagnosis endogenous exophthalmos is difficult in one sided cases. On a question from Jittborg the speaker replied that one would probably always find pathological uptake values with a suppression or stimulation test if an endogenous exophthalmos was present.

Gjone E. *Familial plasma cholesterol ester deficiency*

60% of cholesterol is found as ester. Cholesterol reacts with a fatty acid lecithin. Free cholesterol is found in all the cells of the body however it is deposited in the vessel wall as ester. Three sisters were reported lacking the enzyme LCAT (Lecithin cholesterolacyltransferase). They had low concentrations of lysolecithin and cholesterol ester and practically all cholesterol was unbound.

The disease was manifested by slight proteinuria, normochromous anemia, milk like plasma and low concentration of alpha pre beta lipoprotein. The erythrocytes had a peculiar look because of the high cholesterol content and foam cells were found in the bone marrow and by kidney biopsy. The most striking clinical sign, however, was corneal changes to be described by the next speaker.

Bergaust B. *Corneal changes with familial plasma cholesterol ester deficiency*

The three above mentioned sisters were examined ophthalmologically. Their ages were 13, 37 and 44 years. They had no history of eye troubles and their vision was normal. The same corneal changes were found in all three by slit lamp examination. There was tiny gray dotted opacities centrally in the cornea, then a clear intermediate zone and peripherally denser opacities almost resembling an arcus senilis. Cholesterol was probably deposited in the cornea.

Valebjorg H. *On intraocular feedback mechanisms by intraocular pressure and the physiological basis for the method of tonography*

Kabbe's experiments were reported in which the blood vessels in the ciliary processes were inspected and photographed through a window in the wall of the eye bulb. By increasing the intraocular pressure from 15-20 mm a distinct compression of the ciliary vessels became apparent. Some capillaries closed entirely and in some parts the veins were particularly pressure sensitive. The effect on the vessels increased with rising tension. A discussion followed on the significance this had for the process of tonography and it was agreed that there is little probability that the rise in tension coming when a tension meter is placed on the eye will not influence the production of aqueous humor.

Willemann J. *Thrombocytopenia with Diamox treatment*

A 65 year old woman was reported who had been treated for 3 years with 20 mg Diamox daily for glaucoma. She now had symptoms of severe thrombocytopenia. The condition improved after discontinuing the Diamox. Resuming Diamox treatment resulted in worsening of the condition which was again improved withdrawing the drug. A discussion followed of the usual complications seen under Diamox treatment.

Valebjørg H *Once again on the diagnosis of cataract*

The speaker was against keeping the diagnosis of cataract from the patient as long as possible. The patients had to have an explanation for their reduced vision, and if one told them the situation most of them were relieved.

Discussion Weidemann suggested that one should get away from the word *grønn stær* and call it *glaucoma* as is done in many other countries.

Syrdalen P *Retinal detachment and vitreous bleeding*

In 1967 133 patients with retinal detachment were admitted to the eye department of Rikshospitalet. Eleven had already had one vitreous bleeding and another eleven had signs of vitreous bleeding when received in the department altogether sixteen per cent. The most probable explanation for these vitreous bleedings was described.

In a case of retinal detachment without vitreous bleeding the time from examination by an ophthalmologist to admission is usually less than one week. However if there has first been vitreous bleeding the time is usually several weeks or months. The retinal detachment is hidden by these bleedings and the diagnosis is therefore often made very late. With heavy vitreous bleeding one should therefore always consider the possibility of a retinal detachment. The patient should lie in bed with the head and upper part of the body in an elevated position; the patient should preferably use binoculars. A good view into the eye is usually obtained within a few days.

Discussion Roe pointed out the danger of the macula becoming detached if the patients have their retinal detachment too long. Nyquist mentioned the importance of the patients' subjective symptoms giving some idea of the diagnosis even in those cases where the fundus could not be inspected.

Kolstad A *Can our pilocarpine drops be improved?*

The pilocarpine drops utilized up to now can be improved since they have a low pH value and contain a mercury preparation not seldom giving an allergic reaction. Our pipette bottles are also not good. In cooperation with a medical firm the speaker had produced some drops with pH values of 6.5. At this pH the pilocarpine is found to a larger extent as a not dissociated alkaloid which may increase effectivity. Polyvinyl alcohol was added to the drops. A mixture of EDTA and benzalconium chloride was utilized as conservant. Experience over 2 years showed that the patients felt that these drops were more pleasant to use and on average a somewhat more satisfactory decrease of the intraocular pressure (averaging 3 mm Hg) was obtained.

Discussion Horven asked about the durability of the drops. At 15°C they were stable for three months and at 25°C for one month before a reduction of 10% was observed. It was further discussed whether the present prescription on the pipette bottles that the eye drops should be used within one month after delivery from the chemist was justified. The prescription will probably be omitted.

Bertelsen T *New investigations into fibrillographia epitheliocapsularis so called senile exfoliation*

Earlier electron microscopic investigations were recapitulated. The amorph layer that is demonstrated basally in the lens capsule in the equatorial zone never has a larger continuous extent but is found like islands. The speaker was of the opinion that the exfoliation material originated here.

Discussion Petersen. By slit lamp investigation one can find cases where it is only *fnokk* (i.e. deposits of Busacca) on the part of the pupillary pigmented edge close

jest to the iris stroma (i.e. farthest from the lens) From long term observation it can be seen that these snokk do not move and consequently may be firmly connected with the pigment. Further deep down between the pigment folds can be found a fine white more diffuse layer that can possibly represent the first tiny formation of the exfoliation material. When an enucleated glaucoma eye with exfoliation is examined it is striking how abundant exfoliation material could be spread over the ciliary body and iris and it was not easy to understand how these large amounts of material could be produced by the lens alone. Consequently much could be in favour of the exfoliation material being produced in the pigment epithelial layer in the ciliary body and iris. Bertelsen felt that Petersen laid too much emphasis on the results of the slit lamp examinations. It was much more common to find exfoliation deposits on iris than the impression given from the slit lamp. Examining exfoliation in an autopsy material showed that most exfoliation material was always found on the anterior of the lens. It was possible that the exfoliation material could be produced in more than one place but he did not believe so.

Odland M. *Familial appearance of pigmentary glaucoma*

The characteristic clinical features of this type of glaucoma were mentioned and a family with several cases was reported.

Discussion. Petersen mentioned a 29 year old man with the typical clinical picture. Heavily pigmented trabecular meshwork. After a strong acute rise the tension was normalized and a discussion followed on whether the high tension might have pressed the pigment through the trabecular meshwork and possibly made a sort of drainage because young people have a more elastic trabecular meshwork. Holstad mentioned a patient who got a considerably increased pressure with mydriatics when a large pigment expulsion in the aqueous humor was found. The rise in tension was temporary and subsequently the tension remained at lower values than before the experiment.

Flage T. *Moorens ulcer*

A 67 year old man was reported who had symptoms at first in the right eye. Here the disease worsened in spite of treatment with excision of the ulcer margins and later lamellar keratoplasty. By now signs had appeared in the other eye however here it seemed that Prednisolon had stopped the progression.

Discussion. Dr. Isler reported on a patient with Moorens ulcer in the remaining eye. The symptoms started more than 10 years ago and conservative treatment and a conjunctival flap were tried without success. Then a keratoplasty with auto grafting was performed and the condition remained satisfactory for a long time. There was considerable astigmatism but good vision with contact lens. Signs of a relapse now appeared. Mallig was of the opinion that the disease was not always on both sides. He had followed a case for 30 years. Braathen said that if the little edge with normal retina near the limbus lost the ulcer will never heal. Th. massen mentioned the doubtful prognosis. Neither keratoplasty nor a conjunctival flap will always lead to success however mentioned a case that had been well for six years after lamellar keratoplasty.

Hans Walther Larsen Manual and Color Atlas of the Ocular Fundus Copenhagen Munksgaard 1969 Pp 312 223 color pictures Price D kr 400 - \$ 22 - £ 13 6s - DM 212

This monumental manual and color atlas of the ocular fundus is considered the most elaborate and technically superior presentation hitherto published in its kind

The book consists of two parts the *manual* (p 11 119) with descriptions of the affections of the ocular fundus illustrated in the *atlas* (p 121 301) by 223 color photographs which are accompanied by an explanation and brief clinical notes

This idea of an expansion from the customary limits of an atlas by adding more comprehensive descriptions is certainly a good one and a real engagement at the same time. The author's choice appears optimal regarding the proportions of the manual avoiding the many details belonging to a text book and a unsatisfying too short style. He has succeeded in very precise and adequate descriptions comprising general clinical aspects heredity when indicated morphology with differential diagnosis and histopathology. References of reasonable dimension are to recent literature from accessible sources

The complete separation between the manual and the atlas involves an alternative study of the two parts with much turn over. References facilitates this activity and turn over could not be evaded anyhow. To the reader's comfort the manual is printed on mat paper the atlas on excellent coated art paper

Might the author have competitors in description he again appears master in fundus photography. His previous *Atlas of Diabetic Retinopathy* 1959 and *Atlas of the Fundus of the Eye* 1964 have been of great success and this could but be repeated this time too. The fundus pictures are simply superior. One explanation must be the author's combined command of ophthalmology and the refined technique of fundus photography

All photographs have been taken by the author with a Zeiss Camera or a Nikon Hand Camera on Agfacolor or Kodachrome. Normally the photographs are enlarged 2.5 times the several montage photographs 1.75 times. Ordinarily 30° of the fundus is visualised in the pictures but also some originally of 15° are reproduced

The content is rather complete comprising not only common affections in ample variation but also rare lesions are presented. The normal fundus is well described. Next come congenital variations and disorders affections of the optic nerve and phacomatosis. Fundus changes in vascular diseases are well represented as are fundal representations of other systemic affections as blood diseases and metabolic disorders. 30 pictures of diabetic retinopathy demonstrate the author's still flourishing interest. Further a multitude of degenerative changes inflammatory lesions (posterior uveitis) retinal detachment tumors and injuries

The author's combined efficiency as mentioned obliges the technique and layout involved in the final publishing. These are excellent too

The book demonstrates the long art of ophthalmoscopy impressing and pleasing the observing ophthalmologist himself and the whole medical profession as well. Recommendation to all interested in ophthalmoscopy or interpretation of fundus observations

P Brændstrup

Karl Velhagen Der Augenarzt 2nd revised and extended edition Vol 1 with 300 illustrations some in colour Leipzig Georg Thieme 1969 349 pages Price DM 130 -

That was fast work. The 1st edition of *Der Augenarzt* had hardly been completed before the 2nd edition was on its way. Judging by the 1st volume the second edition is going to be appreciably larger but it is believed that it will not exceed 9 volumes - a complete manual. Possibly the volumes will increase not only in number but also in size. Vol. 1 of the second edition is 140 pages larger than vol. 1 of the first edition. The basic idea is to be maintained but the arrangement of the subjects has been somewhat altered.

Vol. 1 contains the following sections: Morphology (J. Rohen), perception of light physiology (Munje), physiological chemistry (Pau and Graeber), pharmacology (Velhagen), general examinations (Velhagen), diagnostic methods (Heydenreich), visual field studies (Schober), methods of testing perception of light (Comberg and Heydenreich), methods of testing colour sense (Heydenreich).

According to random samples the subjects seem to have been carried entirely up to date, the most recent advances in ophthalmology having been added.

The book has extensive bibliographies, an author index and a subject index and its arrangement is excellent and sound.

Holger Ehlers

J. P. H. Alkemade: *Dysgenesis mesodermalis of the iris and the cornea* (A study of Rieger's syndrome and Peters' anomaly). 206 pages, 73 figures, 6 illustrations in colour, 17 tables. Price: Dutch fl. 54.00. Royal Vangorcum Ltd, Assen, The Netherlands, 1969.

This monograph, the first on the subject, gives a thorough account of the clinical features, genetics and pathogenesis of these conditions, based partly upon the author's personal experience from 15 cases and partly upon extensive studies of the literature (about 450 references).

The main part of the book presents an exceptionally thorough assessment of Rieger's syndrome, Peters' anomaly and the differential diagnostic possibilities being afforded by each. In the last chapter the author's cases are reported.

An excellent author and subject index as well as a detailed list of references make the contents easily accessible to the reader.

The volume is of very attractive appearance and the illustrations are extremely well illustrated. Unfortunately a number of printer's errors have slipped into the text.

Finn Kruse Hansen

Course in Retinal Detachment

The Retina Service Massachusetts Eye and Ear Infirmary will sponsor a course in retinal detachment on May 21 22 and 23 1970 The curriculum will include lectures covering the fundamentals of fundus diagnosis pathogenesis and modern methods of treatment of detached retina Tuition is \$ 125 for practitioners Residents \$ 50 upon application from Department Head Checks are payable to Massachusetts Eye and Ear Infirmary and should be sent to Charles Regan M D Retina Service Massachusetts Eye and Ear Infirmary 243 Charles Street Boston Massachusetts 02114

International Orthoptic Congress

in the International Congress Centre M A I in Amsterdam the Netherlands on 11th 12th and 13th May 1971 The three main themes will be 1) visual acuity 2) the scope of orthoptics 3) squint in disease Any information can be obtained from the Congress Bureau 199 Oudezijds Achterburgwal Amsterdam C the Netherlands

The VIIIth ISCERG Symposium

The VIIIth ISCERG Symposium (International Society for Clinical Electretinography) will be held in Pisa (Italy) on 7 11 September 1970

The main topics will be

- 1) Correlation between histology and electrophysiology of the retina (introduced by Prof W K Noell Buffalo USA)
- 2) Electrodiagnostic procedures in visual pathology of children (introduced by Docent Birgitta Zetterstrom Stockholm Sweden)

Free papers will also be accepted

Information Prof Dr Alberto Wirth ISCERG Symposium 1970
Clinica Oculistica Universitaria 56100 Pisa (Italy)

Society of Eye Surgeons

The International Eye Foundation is pleased to announce the formation of the Society of Eye Surgeons Its purpose is to promote the science of ophthalmic surgery among all peoples and nations Qualified ocular surgeons may apply for detailed membership information and application forms to J H King Jr M D Director The Society of Eye Surgeons 5255 Loughborough Road NW Washington DC USA 20016

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ON THE PROGNOSTIC VALUE OF INTRAOCULAR PRESSURE IN TREATMENT OF RETINAL DETACHMENT

BY

NIELS EHLERS and ERIK ØSTERBY

In 45 cases of retinal detachment Ehlers & Ruse (1967-1969) observed unfavorable results to treatment in cases where the intraocular pressure in the eye with detachment was low or considerably decreased compared with the contralateral eye. The object of the present investigation was to further study this correlation in a larger series of patients.

The material comprised 155 consecutive cases of retinal detachment admitted to the Department of Ophthalmology Århus Kommunehospital in the period Jan 1 1964 to Dec 31 1968. 53 cases were excluded for the following reasons: 19 where surgery was not performed (on case of spontaneous healing), 10 where information as to intraocular pressure was not available, 8 with glaucoma and 18 with various intraocular disorders (uveitis perforating lesions epithelial growth in the anterior chamber diabetic retinopathy and phthisis bulbi).

The remaining 102 cases consisted of 63 women with an average age of 57 years (19-74) and 39 men with an average age of 48 years (11-74). The intraocular pressures were measured by applanation tonometry on the day of admission. The results of treatment were judged on the basis of the hospital records. The operative procedures employed were diathermia cryoapplication, extrac scleral indentation often with Rosengren's silverball or cerclage. The material is presented in Table I column 1. In columns 2 and 3 it is divided into 57 cases where reattachment was achieved and 45 where reattachment was not

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achieved These two groups are almost identical as regards age refraction duration of detachment and number of holes With regard to the extent of the detachment and the operative procedure used, there are more total detachments in the non reattached group and an encircling procedure has often been tried

Table I

	Total 102	Reattached 57	Non reattached 45
<i>Age</i>			
0-20 years	5	1 (2 %)	4 (9 %)
21-40 years	12	3 (14 %)	4 (9 %)
41-60 years	46	27 (47 %)	19 (42 %)
61-80 years	39	21 (37 %)	18 (40 %)
<i>Refraction</i>			
emmetropia + hypermetropia	35	20 (35 %)	15 (33 %)
0-5 D myopia	30	16 (28 %)	14 (31 %)
> 5 D myopia	31	16 (28 %)	15 (33 %)
Afakia	6	5 (9 %)	1 (3 %)
<i>Duration of detachment</i>			
<1 week	31	19 (33 %)	12 (27 %)
1-2 weeks	29	15 (27 %)	14 (31 %)
2-4 weeks	8	4 (7 %)	4 (9 %)
>4 weeks	34	19 (33 %)	15 (33 %)
<i>Number of holes</i>			
0	10	5 (9 %)	5 (11 %)
1	55	33 (58 %)	22 (49 %)
2 or more	37	19 (33 %)	18 (40 %)
<i>Extent of detachment</i>			
1 quadrant	4	4 (7 %)	0 (0 %)
2 quadrants	61	37 (65 %)	24 (53 %)
3 quadrants	23	14 (25 %)	9 (20 %)
4 quadrants	14	2 (3 %)	12 (27 %)
<i>Operation</i>			
Diathermia	29	17 (30 %)	12 (27 %)
Cryopexia	4	4 (7 %)	0 (0 %)
Extrasceral indentation	45	26 (45 %)	19 (42 %)
Encircling procedures	24	10 (18 %)	14 (31 %)

Absolute values for intraocular pressure

Table II shows mean values for intraocular pressure. In the entire series as well as in the two subgroups the mean pressure was significantly lower in the eye with detachment than in the contralateral eye. There are however no significant differences in pressure in either the detachment eye or the contralateral eye between the reattached and non reattached cases.

The observed pressures are low. Moriteru (1960) found a pressure of 13.4 ± 0.1 mm Hg in 265 eyes with detachment. In the present investigation the pressure in the contralateral eye was found to be only 13.3 mm Hg. This is lower than the normal intraocular pressure and compared with the findings of Goldmann (1957) (15.45 ± 0.13 , $N = 400$) significantly lower. Yoshioka & Endo (1966) also state that the ocular tension in the contralateral eye is slightly lower than normal.

Pressure reduction in the detachment eye

In the present material the mean pressure difference of 2.1 ± 0.3 mm Hg was found between the detachment eye and the contralateral eye.

In the group with reattachment a pressure reduction of 1.8 ± 0.4 mm Hg was found. In the group without reattachment 2.5 ± 0.5 mm Hg. The pressure reduction is thus greatest in the group without reattachment but the difference is not statistically significant.

Single measurements of intraocular pressure are encumbered with some uncertainty. Reduced pressure is therefore in the present study arbitrarily defined as a difference between the two eyes of more than 2 mm Hg. The material was thereby divided as shown in Table III. Pressure reduction was found in 40%.

Table II
The mean intraocular pressure in mm Hg in eye with detachment and in contralateral eye

	Detachment eye	Contralateral eye
Total	11.9 ± 0.4	13.3 ± 0.3
Reattached	11.3 ± 0.4	13.7 ± 0.4
Non reattached	10.4 ± 0.6	12.9 ± 0.4

The table shows mean \pm standard error of mean.

In the literature ■ pressure reduction is stated as being present in up to 10% (Huerkamp & Behme 1955, Moritera 1960) ■ frequency also observed in the present study if a pressure difference of 2 mm is not demanded

Table III shows that reattachment was obtained in 40 (65%) of 62 cases with the same or higher pressure in the detachment eye. In the group with pressure reduction 17 (43%) reattached cases were found out of 40. The frequency of healing ■ thus significantly reduced with reduced pressure (χ^2 Yates = 4.06, $P < 0.05$)

A higher pressure was measured in the detachment eye in 14 cases in these reattachment was observed in 7. There were 8 cases with disinsertions of which 4 were reattached. In 2 cases of disinsertion the highest pressure was in the detachment eye. These findings correspond to those in larger series (Huerkamp & Behme 1955)

Discussion and conclusion

In the present material a poorer result of treatment of retinal detachment was observed when the preoperative intraocular pressure was reduced more than 2 mm Hg. As seen from Table I the two groups reattached and non reattached are comparable. There are however more cases of total detachment among the non reattached. Do these cases have a low pressure and are they responsible for the poor results in the group as a whole? This is true to some degree ■ 9 of the 12 cases with total detachment and without reattachment had reduced pressure preoperatively. Among the remaining 33 cases without reattachment there are however still 42% with reduced pressure as compared to only 30%

Table III
Results of treatment of retinal detachment

	Reattached	Non reattached	Total
The same or higher pressure in detachment eye	40	22	62
Reduced pressure in detachment eye	17	23	40
Total	57	45	102

The table shows number of cases

among the reattached cases. The two cases of total detachment that did reattach did not have reduced pressure preoperatively. Kleiner (1933) reported an average pressure reduction of 4 mm Hg in cases of detachment. His Table 3 shows that the pressure reduction among the reattached cases was only 2.5 mm Hg. All pressures given were measured with a Schiotz tonometer. It is not possible on the basis of Kleiner's work to set up a table as Table III in the present paper but among the reattached cases a pressure reduction greater than 2 mm Hg was found in 46%. In the remaining cases where however no direct statement is made that reattachment is not achieved a pressure reduction was found in 60%.

It seems justified to conclude that a relatively lower pressure in the detachment eye is a factor of some prognostic value i.e. reduced pressure compared with the contralateral eye provides poorer prospects for reattachment.

Summary

Among 102 cases of retinal detachment the intraocular pressure was found to be lower in the detachment eye than in the contralateral eye. No significant difference was found between pressures in the reattached and non reattached cases. There was a significantly lower frequency of reattachment ($P < 0.05$) among cases with a pressure reduction of more than 2 mm Hg than among the remaining cases of the material.

References

- Ehlers A & Riise D (1967) On corneal thickness and intraocular pressure. *Acta ophthalmol* 45 809-815.
- Ehlers A & Riise D (1969) Corneal thickness and intraocular tension in retinal detachment. *Acta ophthalmol* 47 957.
- Geldmann H & Schmidt T (1957) Über Applanationstonometrie. *Ophthalmologica* 134 1-4.
- Huekamp B & Behrse H (1957) Die Augendrucklage insbesondere das Glaukom bei ablatio retinae mit Operation. *Graefes Arch Ophthalmol* 156 433-447.
- Kleiner L (1933) Der intraoculare Druck bei Netzhautablösung. *Graefes Arch Ophthalmol* 111 485-506.
- Linco E (1966) Intraocular pressure in retinal detachment. *Acta ophthalmol suppl* 84 101-106.
- Mitsuda Y (1960) Studies of the mechanism of regulation of intraocular pressure in the path of retinal detachment. *J clin ophthalmol (Tokyo)* 14 853-861. Cited by *Excerpta med* XII 1: 1011 (1963).
- Mitsuda Y & Fudo Y (1966) Clinical observations on ocular tension in case of retinal detachment. *J clin Ophthalmol (Tokyo)* 10 123-131. Cited by *Excerpta med* XII (1965).

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LEBER'S DISEASE V

BY

TOVE SEEDORFF

SUMMARY

This is the final of a series of papers reporting attempts to elucidate the heredity of Leber's optic neuritis by following descending female lineage in 70 pedigrees described first by Lundsgård in 1944

The present paper deals with 16 families 4 of which have propagated so abundantly that during continued follow up they must be considered of value in studying the mode of inheritance. The remaining pedigrees are for various reasons not suited for affording particulars about the inheritance of the carrier property. The discussion concerns the possibilities of obtaining an ideal material for determining the carrier rate. As the carrier property is disclosed mainly by manifestation of the disease among the descendants the ideal basis for calculation comprises only women who have got so many descendants that there is ample chance of manifestation. However the study has shown that only a few families reproduce so briskly as to afford a basis for deciding whether the carrier rate is 50% or 100% among the girls born in the female lineage.

The conclusion of the whole study is that in the two families with the best reproduction the carrier rate among the women born in the female lineage is higher than 50% among reproductive women 100%. This seems so clear that it cannot be interpreted as a chance accumulation of carriers. The other pedigrees do not include examples militating definitely against this interpretation. 100% carriers among the daughters of carriers and healthy men is not in

accordance with Mendelian proportions. It is uncertain therefore whether the trait of Leber's disease is chromosomal. Thereby it is also uncertain whether this trait may be expected to have same stability as a gene. This combined with a wish to see further examples of briskly reproducing families which may confirm the result is the reason why the author does not consider the finding of 100% carriers among the carriers' daughters as being an established general rule for all families with Leber's optic neuritis.

Introduction

The following 16 pedigrees will be described more briefly than in the previous papers. Information about who first published the individual cases will be omitted. This will facilitate the reading to those who do not have access to the original material. In more thorough studies however it will make a comparison with Lundsgård studies rather more difficult. The method of the study has been described previously and will be supplemented here only by characteristic features of the course of the study. Case histories will be given only if they differ from the expected course or if the case has been interpreted temporarily as some other disease of the optic nerve. Comments to the individual pedigrees comprise a criticism of the pedigree as a basis for calculation or a criticism of the knowledge concerning the number of manifestations. In pedigrees B, E, F and T examples are adduced which elucidate the criterion of non-carrier. In the final discussion the present state of the total material is described as a result of a clinical testing of a number of genetic theories which have been summarized previously (Seidorff 1968). It is pointed out that a teamwork by geneticists, statisticians, pathologists, physiologists, biochemists, neurologists and ophthalmologists is needed to solve the questions still attaching to the disease.

Pedigree B

Method

In the first review of the pedigree in 1961 only one new case was found, B 131 who had developed the disease already while Lundsgård was preparing her thesis. In 1964 a new case was reported from the Gentofte Hospital, Copenhagen. This proved to be B 130. In 1968 inquiries were sent to a few persons of the 5th and 6th generations and to practically all of the 7th generation. The reply rate was fine in Denmark, but no replies were received from U.S.A. The 1968 review did not bring to light any further cases.

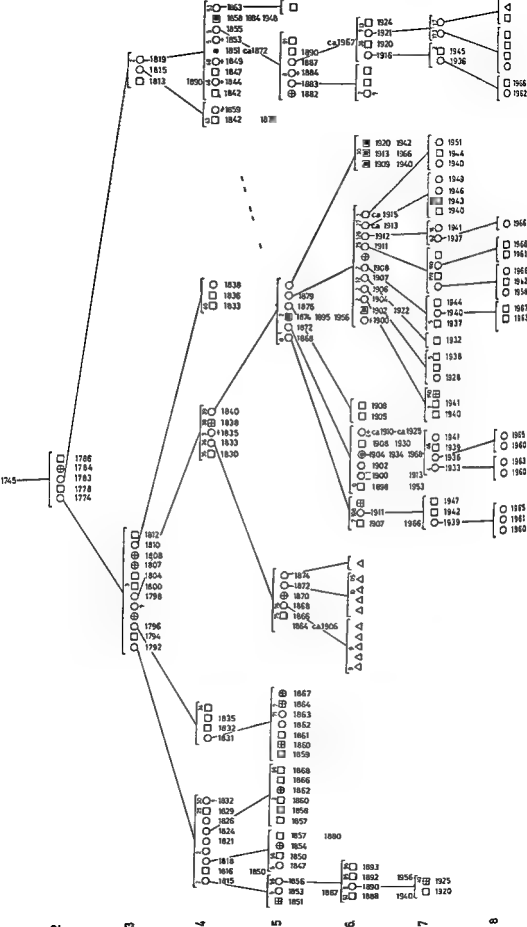


Fig 1
1 ed 8 = B

Results

The pedigree now comprises 192 persons having been supplemented by 55 persons of the youngest generations

Those branches which comprise descendants of B 39 and B 51 have been easiest to follow. They include the 2 new patients both of whom have typical histories and both of whom have been admitted to hospital during the developmental stage of the disease

B 130 M J born 30.4.1913 Gentofte Hospital admitted to the Eye Department on 3.10.1966.

B 131 S J born 16.1.1920 Eye Department Rigshospitalet University of Copenhagen (19.1949) admitted on 2.1.1942

Moreover 2 cases of colour blindness were found (B 136 and II 138)

As to the value of the data concerning the unaffected persons

B 90 has been living in Iowa where he ran a farm with his brother. It is not known whether he is alive or whether he has good vision.

B 91 also lived in Iowa and as far as is known he had good eyesight until his death around the age of 70. He visited Denmark the year before he died but unfortunately the author did not know he was here.

B 92 has been living in America and nothing is known about him.

B 96 answered in 1961 that his eyesight was good and that his brothers had had normal eyesight until they died.

B 107 died at 59 years of age very isolated and unfortunately there are no definite data about his sight.

B 110 emigrated to America in his youth. He had good eyesight until his death and had always been in close touch with the family in Denmark.

B 116 replied in 1961 and 1963 for himself and his brother that both had good eyesight.

B 133 and 134 are presumably living in USA. Nothing is known about them apart from their surnames. Their mother and grandmother are living in California.

B 136 answered in 1968 that he had good eyesight but was colour blind.

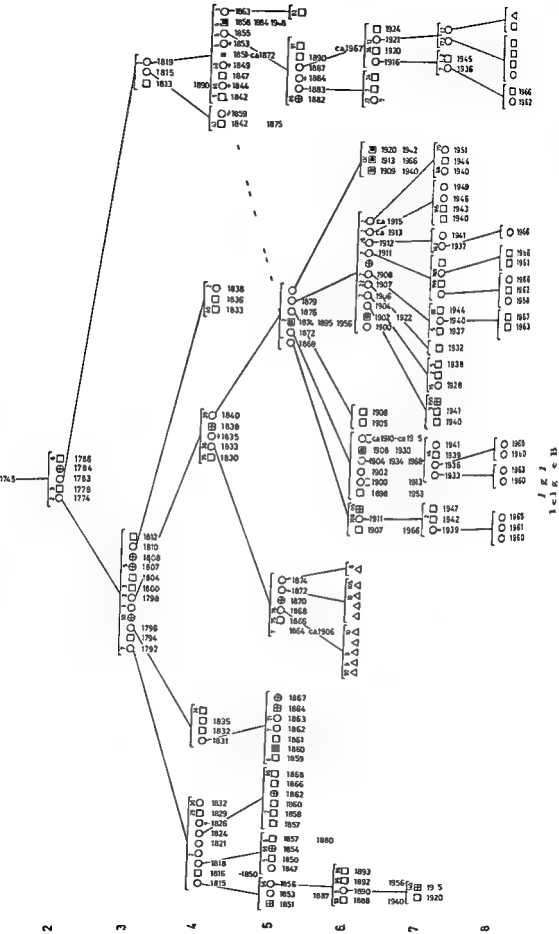
B 138 attended for examination. His vision in both eyes was 6/6 he had no scotoma for white 1/1000 but was entirely red green blind when tested with Ishihara plates.

Among the descendants of B 84 migraine is considered a familial weakness affecting many. The study did not include the frequency of migraine but spontaneously it has been stated that II 120 II 126 B 127 II 157 and B 162 are sufferers and presumably there are others.

The following factors reduce the value of the pedigree

Among the descendants of B 7 there are two contemporary persons B 36 and II 139 both healthy. Unfortunately they do not know the name of II 7 and thus cannot confirm that the study is on the right track. Only manifestation of the disease will be able to confirm this. Nevertheless if B 139 reaches the age of 60 without developing the disease it must be considered reasonable to designate B 7 as non carrier.

The complete data of the christening of B 57 73 are available. These persons were born in Southern Jutland during the interval between the two Dano German wars in 1849 and 1864 but their fate is unknown presumably as a consequence of the moving of the frontier. Complete christening data have also been found for B 74 79 and mar



the predisposed persons gradually as they become 60 in the eye department closest to their homes

Pedigree E

Results

This pedigree now comprises 64 persons 23 women and 39 men. It has been supplemented by 5 persons of the youngest generation. One new case has been found and thereby a new carrier has been demonstrated. The new patient is

E 43 H H L L. born 1917. This patient has been in the Mental Hospital Midelfart for a number of years with schizophrenia. His eyesight was considered normal by his family as well as by the hospital staff because his orientation in the ward was normal. On occasion of the present study he was examined in 1963 by the hospital ophthalmologist who found bilateral atrophy of the discs, normal pupillary reactions and normal tension. His mental state excluded any collaboration on his part so that it was not possible to determine vision and visual field. Nor could he state his own opinion of his eyesight.

Comments: Although the developmental stage of the disease was not observed and cannot be dated, the familial predisposition makes Leber's disease the most likely diagnosis.

Re value of symbols for healthy males

The males of the sibship in the 2nd generation were born in Schleswig Holstein. Possibly they have lived in Copenhagen for some time but later moved to Germany. Therefore we have no data about their vision. The carrier E 6 was born in Copenhagen and married a Danish citizen. Her sons, the men of the 3rd generation, emigrated and died in Germany, Havana, Glasgow and Australia respectively. Accordingly nothing is known about the vision of E 8, 9 and 13. E 12 who was a grocer in Glasgow visited Denmark in 1877 and on this occasion consulted an ophthalmologist. Therefore we know that he was suffering from the disease. It is not until the 4th generation that the symbols for healthy male are reliable.

There are 8 manifestations of the disease in the pedigree. The 4th generation is ready for calculation. The disease has been recorded in

76% of the boys born in the 4th generation (3 out of 19)

38% of the boys who lived to be 10 (5 out of 13)

44% of the men who lived to be 60 (4 out of 9)

There are 6 carriers in the pedigree. The 3rd generation may be counted out of a total of 4 women, one was undeterminable and 3 were carriers.

The 3 carriers have had a total of 9 daughters, 5 of whom were undeterminable, 7 carriers and 2 are under observation. In other words, more than half the women of the generation under observation are undeterminable.

Colour blindness is present in this pedigree. E 12 and E 23 have reported that they were colour blind before they developed Leber's disease. According to information from their next of kin E 33 and E 41 were also colour blind and III 26 states that he is colour blind.

riage data for B 76 and 78 but unfortunately the knowledge that Lundsgård had of the offspring of B 76 78 and 79 has been lost

Among the sibship B 45 53 the females B 50 51 and 53 emigrated to USA B 51 went in 1890 leaving one of her children the daughter B 89 in Denmark. Therefore B 89 and her descendants are Danish while the remaining of the listed descendants of B 51 and B 53 are living or have been living in USA The names and addresses of a number of the family members in USA are known but they have not replied in queries

B 56 and B 83 now have each 2 male descendants who have reached the age of 60 without having developed the disease It must be reasonable therefore, to consider them non carriers

Comments

There is nothing in pedigree B to militate against Leber's disease being inherited according to Mendelian proportions But owing to its incompleteness and the consanguineous marriage of B 39 and B 45 this pedigree does not give satisfactory information about the mode of inheritance of Leber's disease Its main value is that the descendants of B 84 afford a good observation material If manifestations appear among them this will occur within the next few years The fact that the women of this branch suffer from migraine which perhaps bears an unknown relation to Leber's disease lends further interest to this observation material

How the two cases of colour blindness have entered the family cannot be decided on the basis of the data at hand There is no information concerning colour blindness among the ancestors

This is the first time the material presents women who are by way of being considered non carriers - It was the experience from pedigree A which gave rise to a presumption that a criterion of non carriers could be set up The 5th and 6th generations of pedigree A include boys in 11 sibships In 10 of these sibships the eldest son is affected while the eldest son of the 11th sibship is healthy Thus at the completion of studying pedigree A it seemed reasonable to consider a woman as non carrier when her two oldest male descendants have reached the age of 60 without developing the disease However examples from pedigrees E G and T show that this criterion does not hold as the woman may be a carrier nevertheless Therefore the criterion of non carrier is uncertain Unfortunately the fact is that the more male descendants are demanded before a woman is declared non carrier the more undeterminable women will be found in the pedigrees It was considered to introduce a special symbol for a woman having two 60 year old male descendants with good vision to keep an eye on such women in particular Regrettably the persons in question have not been examined by an ophthalmologist and therefore this symbol has not yet been introduced In the future this drawback may be remedied by examining

the predisposed persons gradually as they become 60 in the eye department closest to their homes

Pedigree E

Results

This pedigree now comprises 64 persons 25 women and 39 men. It has been supplemented by 5 persons of the youngest generation. One new case has been found and thereby a new carrier has been demonstrated. The new patient is

E 45 H H L. L. born 197 1905. This patient has been in the Mental Hospital Midelfart for a number of years with schizophrenia. His eyesight was considered normal by his family as well as by the hospital staff because his orientation in the ward was normal. On occasion of the present study he was examined in 1965 by the hospital ophthalmologist who found bilateral atrophy of the discs, normal pupillary reactions and normal tension. His mental state excluded any collaboration on his part so that it was not possible to determine vision and visual field. Nor could he state his own opinion of his eyesight.

Comments: Although the developmental stage of the disease was not observed and cannot be dated, the familial predisposition makes Leber's disease the most likely diagnosis.

Re value of symbols for healthy males

The males of the 1st generation in the 2nd generation were born in Schleswig Holstein. Possibly they have lived in Copenhagen for some time but later moved to Germany. Therefore we have no data about their vision. The carrier E 6 was born in Copenhagen and married a Danish citizen. Her sons, the men of the 3rd generation emigrated and died in Germany, Havana, Glasgow and Australia respectively. Accordingly nothing is known about the vision of E 8, 9 and 13. E 10 who was a grocer in Glasgow visited Denmark in 1877 and on this occasion consulted an ophthalmologist. Therefore we know that he was suffering from the disease. It is not until the 4th generation that the symbols for healthy male are reliable.

There are 8 manifestations of the disease in the pedigree. The 4th generation is ready for calculation. The disease has been recorded in 76% of the boys born in the 4th generation (5 out of 19), 35% of the boys who lived to be 10 (3 out of 13), 44% of the men who lived to be 60 (4 out of 9).

There are 6 carriers in the pedigree. The 3rd generation may be counted out of a total of 4 women, one was undeterminable and 3 were carriers.

The 3 carriers have had a total of 9 daughters, 5 of whom were undeterminable, 2 carriers and 2 are under observation. In other words, more than half the women of the generation under observation are undeterminable.

Colour blindness is present in this pedigree. E 17 and E 25 have reported that they were colour blind before they developed Leber's disease. According to information from their next of kin E 35 and E 41 were also colour blind and E 56 states that he is colour blind.

lineage were born in the 5th generation of pedigree E during the period 1899 to about 1930. For the time being this material has been put aside.

Comments

Three carriers in one sibship may be a chance accumulation. The high incidence of carriers must repeat itself in the subsequent generations before the pedigree can afford the desired information concerning the mode of inheritance.

E 11 was found to be a carrier in 1936 when her eldest daughter's son developed the disease. She herself had 4 sons who were healthy including 2 who had lived to be about 75. Had E 11 not had this daughter she might have been taken to be non-carrier.

Pedigree F

Results

This pedigree now comprises 93 persons: 37 males, 54 females and 2 of unknown sex. It has been increased by 44 persons. One new case has been found in the youngest generation and this disclosed 3 carriers.

Eldest son of F 62: A. F. II born 24.4.1943. Dept. of Neurosurgery, Rigshospitalet, University of Copenhagen 563,0/1965; admitted 6.12.71 19.1965.

In September 1965 the patient had noticed blurring before the left eye and one week later also before the right eye. Examination at the Central Hospital, Næstved in November 1965 showed the vision in the right eye to be 3/60 and in the left eye finger counting at a distance of 0.5 m. Ophthalmoscopy: Pale disc on the left. Visual field: Outer limits normal. EEG: Suspicion of a focal lesion in the right occipital lobe. Accordingly he was transferred to Rigshospitalet, Department of Neurosurgery and on 8.12.1965 he was examined in the Eye Department, Rigshospitalet, Tagensvej. Vision in right eye 6/40 in left eye finger counting at a distance of 10 cm. Visual field of right eye: Quadrant c anopsia superotemporally; central scotoma of 10°. In addition, endocrine signs such as decreasing libido and weight gain. There was thus indication for exploratory craniotomy with a view to a tumour in the region of the chiasm. At operation the optic nerves were found to be slightly injected, perhaps somewhat thinner than usual but not definitely abnormal. Arachnoid adhesion was found below and anterior to the chiasm. After the operation the vision in the right eye was 1/30 and in the left eye finger counting. Diagnosis: Bilateral optic neuritis. The patient was then referred to the State Institute for the Blind and Weak-sighted where by chance he was examined by the present author. Since at that time pedigree F had been studied his relationship to family F could soon be disclosed. The patient himself was unaware of the predisposition. The correspondence had been with his maternal grandmother 3 years previously.

The following data will be given to elucidate the value of the symbols for healthy male among the descendants of F 14.

According to information from their sister F 33 F 30, 31 and 34 had good eyesight until they died at 40 or older. F 45 had good eyesight at 60 according to his

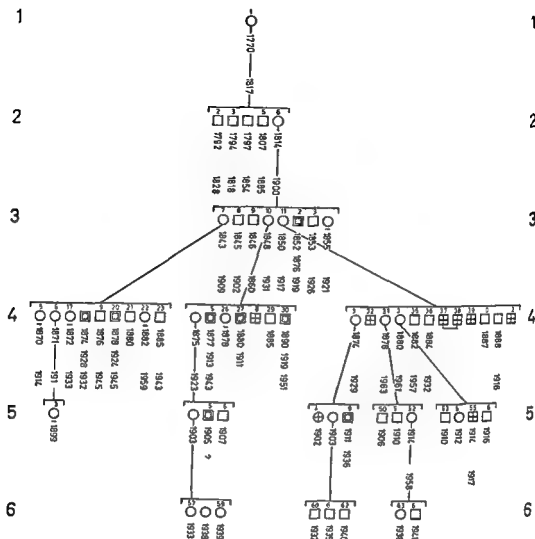


Fig 2
Pedigree E

The colour blindness has entered the family through the progenitor E 1's husband. He had come to Copenhagen from Schleswig Holstein because he had been the queen's physician in ordinary from her youth and he became professor to the University of Copenhagen. He corresponded with Goethe and on occasion of Goethe's *Farbenlehre* he wrote him a letter in 1811 which Goethe published. In this letter he described his impression of the colours of silk of the sky flowers minerals and jewels paintings oleum ricini and of the patients skin. In his own opinion he was suffering from violet blindness *akyanoblepsie* but he wrote among other things that the redness of the sky was merely a thing he knew from reading and that he was unable to distinguish white silver ore from red. Thus his colour blindness might also have been red blindness.

Violet blindness is so rare that the family would be worth a further study. At the same time the male lines could be reviewed for Leber's disease. Therefore the persons of the male lineage are recorded 48 persons including the 14 from the pure female

sister F 44 and this same sister stated that F 52 54 and 56 have good vision in 1969 - now aged 67 64 and 60

The pedigree includes 8 carriers (3 of whom were also affected) The 4th generation is ready for calculation of the carrier rate Among descendants of F 14 5 girls had been born 2 of whom were undeterminable and 3 carriers (one of whom was affected as well) The 3 carriers have a total of 7 daughters 1 of whom are undeterminable and 3 carriers (including 2 affected) and 3 are under observation Thus in the 6th generation the incidence of undeterminable may get as low as 1/7

Comments

3 carriers in the sibship F 27 - F 34 may be a chance accumulation A high carrier rate must manifest itself also in the subsequent generations to be convincing

F 33 was considered non carrier until 1966 At that time she had 2 sons who had reached the age of 60 without developing the disease And then the disease manifested itself in the eldest son of her eldest daughter's eldest daughter Later a third of her sons has reached the age of 60 without developing the disease Thus the criterion of non carrier must be more exacting than first assumed and will thereby become so strict with a view to the demanded number of descendants that it can hardly be fulfilled with the size of the present day Danish families

Pedigree H

Results

This pedigree has been augmented by 7 persons of the youngest generation No new cases have been found In the 6th generation there are two brothers H 31 and H 32 who have reached an age over 60 and who are listed as unaffected The elder one H 31 emigrated to America in his youth and none of the living members has any news of him H 32 stated in a letter in 1964 that his eyesight was good All other men of this pedigree were younger than 60 when the study was closed

H 21 is the oldest carrier and she is the progenitress of that part of the pedigree which is of any importance As to the older persons of this pedigree it is known only that they have existed not whether or not they were affected

Comments

With 4 carriers pedigree H is too small to afford any particulars concerning the mode of inheritance but the younger generations make up quite a good material for observation

Comments

The pedigree includes only 3 carriers viz the mother maternal grandmother and great grandmother of 2 probands Such a pedigree cannot elucidate the mode of inheriting the carrier property

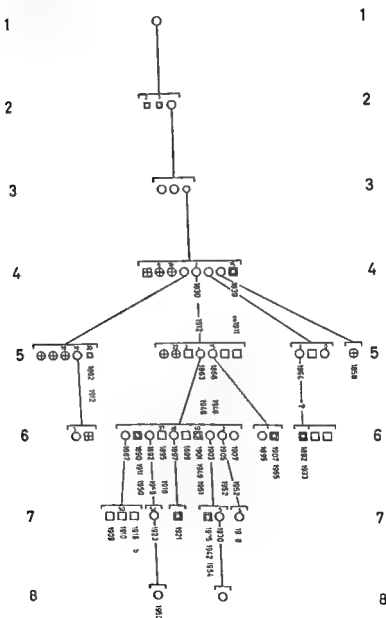


Fig 5
Pedigree k.

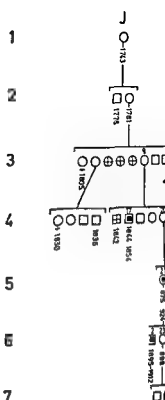
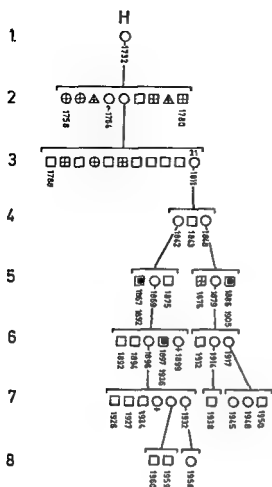


Fig 4
Pedigree H and J

Pedigree J

Results

This pedigree is unchanged since the study of Ruth Lundsgård J 22 cannot be traced J 23 lived in Canada already when Lundsgård was performing her study and her sons are presumably living there too J 24 emigrated to Canada in 1957 Thereby the possibilities of finding living members of the family in Denmark have been exhausted Not much is known about the men listed as unaffected in the 4th generation as they had died before Lundsgård's study According to Lundsgård J 15 must have had some eye trouble because he was said to have always worn dark glasses For J 18 the observation period was only 20 years since at that age he was blinded by an explosion accident J 9 is the progenitress of that part of the pedigree which is of any importance

A 51 C A J J born 31 8 1916 Odense County and City Hospital Dept of Neuro surgery case rec 3 0/1960 61 Admitted as an emergency to the Neurological Dept on 24 10 1960 with right sided hemiparesis At admission his next of kin reported a family history of an eye disease causing blindness appearing at the age of 30 50 Oph thalmoscopy Discs well defined well vascularized non congested Visual field Presumably right sided hemianopsia Right pupil larger than the left Bilateral carotid angiography and left sided vertebral angiography Obstruction in the left int carotid artery but not suggestive of thrombosis On 26 10 the patient was transferred to the Dept of Neurosurgery with severe right sided hemiparesis pharyngeal paresis and total aphasia Diagnosis Occlusion (kink) of left internal carotid artery 44 453 The case was likened to one described by Quinlebaum in 1959 On 29 10 resection of the left int carotid art Control X ray on 27 11 however showed total obstruction at the site of resection On 7 12 exploration at the site The lumen distally to the site of operation was filled with organized thrombotic masses It proved impossible to re establish the flow through the vessel

In February 1965 the author visited the patient on occasion of the present study He was in a nursing home ambulatory and able to feed himself He was friendly and cooperative apparently understood the object of the visit but was severely aphatic being able to utter only yes and no and count to three Vision Questionable perception of light Ophthalmoscopy Total atrophy of the discs on both sides

Comments It is not known when the atrophy of the discs set in presumably during the months after discharge from hospital The severe optic atrophy cannot be explained solely by the carotid thrombosis and it is also not characteristic of Leber's disease As a questionable case this patient is labelled by the symbol for unaffected male

When considering this matter with regard to his mother A 34 she is among the whole family the only woman with male descendants to be a non carrier Accordingly it is very difficult to defend the view that her son's disease has no relation to Leber's disease Another 2 sons had good vision in 1965 They have now almost reached the age of 60 and then there will be an indication for a repeated examination

This pedigree includes 8 carriers A 1 being the oldest

The 4th generation is ready for calculation 6 women were born 4 of whom are undeterminable and 2 carriers

The 5th generation is also ready now 11 women were born 8 of whom are undeterminable while 3 are carriers

The 6th generation is under observation 8 women have been born 3 of whom are undeterminable 2 are carriers and 3 are under observation

Comments

Owing to the large number of undeterminable women reserve has to be displayed in advancing any conclusions

Pedigree L

Results

This pedigree has been supplemented by a sibship in the 4th generation but

Pedigree K

Results

This pedigree now comprises 58 persons 35 females and 23 males It has been increased by 3 persons Before K 54 Lundsgard had listed a person who has now been deleted Three new cases of Leber's disease have been found apart from one case of bilateral optic nerve atrophy due to another cause

K 40 R G F N born 28 I 1901 Admitted to the Eye Department of the St Joseph Hospital Odense from 5 I 2 1949 to 21 I 1950 The visual impairment had started in the left eye in Oct 1949 in the right eye a few days before admission The course was typical and the patient was aware of the familial predisposition at admission

K 45 A C M A born 22 4 1907 Admitted to the Eye Department of the Arhus Municipal Hospital (5538/65) from 18 3 to 30 3 1965 The visual impairment had started in Jan 1965 in both eyes and the patient was admitted when he could no longer read One year previously he had had nerves because of overstrain In respect to possible poisoning it was known that in the autumn of 1964 he had worked one day on melting lead He reported smoking 3 packs of cigarettes a week and drinking 6-7 pints of beer and a couple of gins a day Since last New Year he had been slimming and had lost 10 kg In addition during the past few months there had been tingling and a sensation of cold in the two ulnar fingers especially on the right Ophthalmoscopy revealed signs of optic neuritis and examination of the visual field showed a central scotoma for white On the basis of the history and because the patient was almost 57 years of age it was had reached an age at which manifestation of Leber's disease is generally not expected the condition was diagnosed as tobacco alcohol amblyopia

In April of the same year the author visited the patient on occasion of the present study and realized that he was affected with Leber's disease

Comments Knowledge of a predisposition makes the diagnosis Leber's disease more likely than tobacco amblyopia As a matter of fact the pathogenesis is still so obscure that you can just as well choose the viewpoint the causes perhaps have been collaborating

K 53 C W W born 16 9 1921 Admitted to the Eye Department of the Odense County and City Hospital 5 10-12 10 1953 The patient was aware of the familial predisposition at admission Vision had been deteriorating in the left eye during the past months and he was admitted when the right eye became involved The signs and course were typical

Re symbols for healthy male

In the 5th generation there are 5 men 3 of whom K 20 K 21 and K 29 emigrated to USA According to Lundsgard K 20 developed an eye disease at the age of 50 K 27 was a farmer and minor business man in Utah while nothing is known of K 29 K 23 was originally a baker but later worked in a biscuit factory died at 74 K 26 was originally a weaver but later became caretaker died at 90 In other words the change of occupation by the latter two at a fairly advanced age might be explained by a visual loss However in 1965 a son of their sister's stated that both had had good eyesight until they died In the 6th generation there are 4 symbols for unaffected male K 31 who died young K 39 who was examined in 1965 and had good vision and lastly K 41 and K 48 about whom nothing is known

K 51 occupies an exceptional position since at the age of 44 he developed bilateral total atrophy of the optic nerve of a complicated genesis

h 51 C. A. J. J. born 31.8.1916 Odense County and City Hospital Dept of Neurosurgery case rec 510/1960 61 Admitted as an emergency to the Neurological Dept on 24.10.1960 with right sided hemiparesis At admission his next of kin reported a family history of an eye disease causing blindness appearing at the age of 30-50 Ophthalmoscopy Discs well defined well vascularized non congested Visual field Presumably right sided hemianopsia Right pupil larger than the left Bilateral carotid angiography and left sided vertebral angiography Obstruction in the left int. carotid artery but not suggestive of thrombosis On 26.10 the patient was transferred to the Dept of Neurosurgery with severe right sided hemiparesis pharyngeal paresis and total aphasia Diagnosis Occlusion (kink) of left internal carotid artery 44453 The case was likened to one described by Quattlebaum in 1959 On 9.10 resection of the left int. carotid art Control X-ray on 27.11 however showed total obstruction at the site of resection On 12 exploration at the site The lumen distally to the site of operation was filled with organized thrombotic masses It proved impossible to re-establish the flow through the vessel

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Comments

Owing to the large number of undeterminable women reserve has to be displayed in advancing any conclusions

Pedigree L

Results

This pedigree has been supplemented by a sibship in the 4th generation but

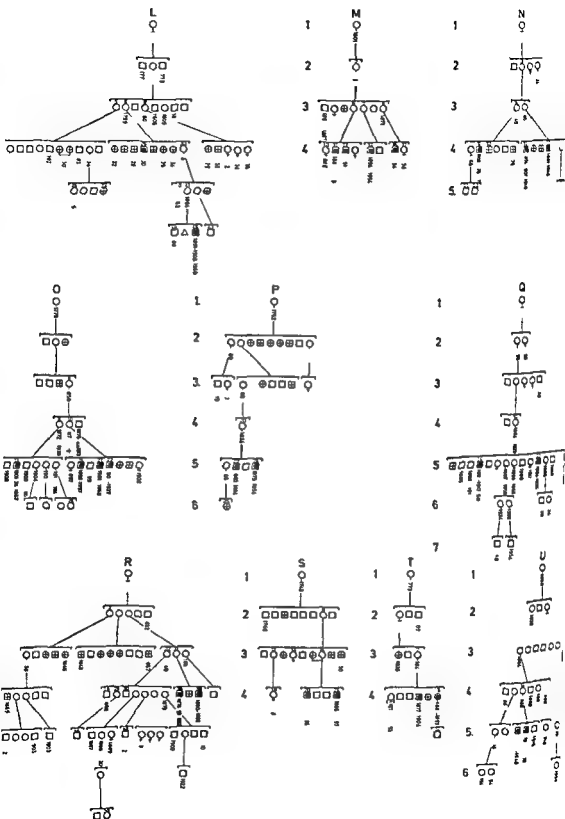


Fig 6
Pedigree L M N O P Q R S T and U

could not be supplemented by any contemporary persons and no new cases of Leber's disease have been detected. Much genealogical work has been done unsuccessfully to trace contemporary persons but the knowledge of the sibships L 13-92 and L 31-35 is still restricted to christening data and the knowledge that Lundsgård had of the sibship L 36-39 has now been lost. The disease has been demonstrated only among the descendants of L 6 and among them the female lineage is now extinct, half her descendants having died in childhood. L 44 answered an inquiry in 1965 to the effect that he and his male cousin L 41, also still alive, had good eyesight.

Comments

In pedigree L there is nothing to militate against the carrier property being transmitted in Mendelian proportions.

Pedigree M

Results

It has not proved possible to get into touch with any person of pedigree M. The pedigree has not been supplemented and no new cases of Leber's disease have been detected.

The code data recorded by Lundsgård were not sufficient to trace the records. The code data for M 14 referred to the New York Eye and Ear Infirmary which has not been asked. M 16's address could be traced until 1936. M 10, M 13, M 15 and M 17 are entirely unknown. The descendants of M 13 had been lost trace of even before Lundsgård's study.

Comments

This pedigree was finished in 1944. As there is only one proband it is fairly valuable. The 3rd generation may be included in the calculations. Of the 6 girls born in the 3rd generation 3 have had children and all have proved to be carriers. However this is too uncertain a basis for altering the views on the laws of inheritance.

Pedigree N

Results

All 3 patients of this pedigree had died before the present study was started. It has not been possible to supplement the pedigree and no new cases have been detected.

Nothing is known about the ■ brothers of the youngest generation Their mother married in Germany and presumably all three have remained German. There are 3 carriers in the pedigree a mother and her 2 daughters 5 women have been born in the 4th generation all undeterminable

Comments

This pedigree is unsuited for assessing the mode of inheritance of the carrier property

Pedigree O

Results

The pedigree has been supplemented by 4 persons of the youngest generation and 2 new cases of the disease have been detected

O 19 H V F H (B) born 11 7 1898 Admitted to the Eye Department of the Copenhagen City Hospital (413/1955) 20 5 14 6 1955

The visual impairment had set in 5 weeks before admission Vision in right eye 6/12 in left eye 1 2/60 Visual field Relative central scotoma for red of 10° on the right absolute central scotoma of 20° on the left Ophthalmoscopy Normal findings Pncu moventriculography showed a small questionable impression into the anterior wall of the 3rd ventricle On 18 7 1955 therefore the patient was transferred for craniotomy to the Department of Neurosurgery Bispebjerg Hospital Operation showed a slightly thickened but not definitely abnormal arachnoid around the chiasmal cistern The optic nerves and chiasm were not involved but the optic nerves were somewhat whiter than normal

Comments The pneumoventriculographic appearances afforded the indication for operation As is apparent from Lundsgård's thesis there was a similar change in the anterior wall of the 3rd ventricle in O 22 (Case 89) who developed the disease in 1934 and arrived for craniotomy at Rigshospitalet University of Copenhagen in 1935

O 21 A A S H born 9 9 01 57 years old waiter since 1930 suffering from anosmia after a cranial fracture since 1940 from hypacusis after otitis Jan 1958 he got a blow of a fist on the back of the head 14 days later visual impairment started in the right eye 1 2 58 he was seen in the Eye Department in Næstved from where he was referred to the Military Hospital Copenhagen 12 3 58 Vision right eye 2/60 left eye 6 6 c corr Field of vision upper bitemporal quadrantanopsia involving right centre Oph thalmoscopy swelling of the discs with slight protrusion blurring of the margins dilated veins and hemorrhages at the margins At this moment symptoms seemed to show intracranial pressure but the history of the family was wellknown 21 3 hemorrhages and venous stasis had disappeared leaving only a blurring of the disc margins and the diagnosis of Leber's disease was accepted Neurological examination was performed but the record could not be found Vision each eye in oct about 1/60 exc fix

This pedigree includes only 3 carriers In the 5th generation there are 6 women 3 of whom are undeterminable and 3 under observation

Comments

The pedigree is still too small to afford any contribution to a conclusion concerning the mode of inheritance

Pedigree P

This is an old pedigree. The youngest patient was born 85 years before the present study was started. The 2 patients have not been traced and the pedigree cannot be supplemented. It includes only one carrier and is too small to give any information about the mode of inheritance.

Pedigree Q

Results

Supplemented by 2 persons of the youngest generation. One case has appeared.

Q 2: A V J, born 1961/11. This patient had spent 3 years in a German concentration camp. The visual impairment started in 1946 and on 16/10/1948 the patient was examined in the State Institute for the Blind and Weaksighted. It is apparent from the records of this Institute that he had first been admitted to the Århus Municipal Hospital and to the Neurological Department of Rigshospitalet, University of Copenhagen where his condition was diagnosed as bilateral retrobulbar neuritis disseminated sclerosis and nervousness due to imprisonment. At the Institute for the Blind and Weaksighted the family was well known and here the disease was diagnosed as Leber's disease.

There is only one carrier in this pedigree. Among her 6 daughters 4 are undeterminable while 2 are still under observation.

Comments

The pedigree is too small to give any information about the mode of inheritance.

Pedigree R

Results

Pedigree R is a large one built up around two patients and their mother who is the only carrier of the pedigree. The patients born in 1846 and 1880 had no doubt died before the present study was started. It has not proved possible to supplement the pedigree and it is entirely unchanged since Lundsgård's publication. Knowledge of R 1 and R 4 and of the descendants of R 3 has been re-established but is based exclusively upon archive studies. Lundsgård also

knew of the descendants of R 2 through archive studies and moreover she had among the descendants of R 20 such substantial knowledge of the persons living around 1940 that she considered R 20 to be a non carrier R 20 and her descendants have now been completely lost to follow up

Comments

In her chapter on mutations Lundsgård interpreted R 21 as the woman in whom a mutation had arisen stating that the gene disappeared already within one generation because the progenitress (R 21) did not have daughters

The questions whether R 4 already was a carrier and R 20 thus was a healthy daughter of a carrier and whether R 20 was in fact a non carrier cannot be further elucidated and the pedigree cannot be supplemented unless new patients crop up

Pedigree S

Pedigree S is an old one dealing with two brothers who developed Leber's disease before the turn of the century and who must have died long before the present study was undertaken This pedigree has only one carrier It has proved impossible to find descendants of her sisters No information is to be had concerning the mode of inheritance

Pedigree T

Pedigree T is also an old one with one carrier and two patients The latter of these two cases occurred 55 years before the present study was started and neither patient could be traced The female lineage is extinct and the pedigree is unchanged since Lundsgård's study

Comments

The distribution of manifestations in sibship T 8 - 13 is very unusual The three eldest children are healthy the two sons even had good eyesight until they died at a ripe old age If T 7 had belonged to a larger pedigree and if she had had only the three eldest children she might have been interpreted as a non carrier However her youngest daughter developed Leber's disease at the age of only 11½ years

Pedigree U

Results

The pedigree has been augmented by 3 persons of the youngest generation all females. No new cases have manifested themselves and thus the pedigree still contains only 2 patients and one carrier.

Comments

In its present shape this pedigree tells us nothing in respect to the mode of inheritance of Leber's disease.

Size of the Total Material

The entire material was entered on a card index system. This card index comprises persons whose accurate birth date is known. Children who died before the age of 10 were excluded. The index gives the actual figures relating to the size of the material i.e. the number of persons identified by complete data. It is not applicable direct as a basis of calculations regarding the mode of inheritance because it includes everybody also persons whose fate is unknown and branches of the families that can no longer be traced.

The birthday index was used as a basis of Fig. 7 which affords information about the total size of the material and the number of patients. It will be seen that each year about 2-3 females and 2-3 males have been born.

Annual Number of Manifestations

In Fig. 9 the times of manifestations are tabulated to show how many manifestations occur annually. Since 1890 up to 2 manifestations have occurred each year.

Empirically however more than two cases of the disease arise annually in Denmark and thus there appear to be other families with optic neuritis than those included in this study. Concurrently with the present study the author has investigated because of reports of new cases 5 families with sporadic cases of the disease and 10 families in which the disease appears to have developed in only one isolated case. In other words since 1960 a larger number of notified cases have proved to have no connection with Jundsgård's pedigrees than those appearing in the families. The files of the University Institute of Human Genetics (Copenhagen) also include a number of reports on cases from the pe-

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	Males			Females		
	Age at manifestation per 1000	Age at manifestation per 1000	Age at manifestation per 1000	Age at manifestation per 1000	Age at manifestation per 1000	Age at manifestation per 1000
1860-69		3	3		2	2
1870-79		3	3			
1880-89		8	8			
1890-99	7	6	13			
1900-09	7		7	3	1	4
1910-19	12	3	15	1		1
1920-29	10	1	11	4		4
1930-39	22		22	2		2
1940-49	8		8	5		5
1950-59	16		16	1		1
1960-69	11		11	1		1
total	93			17		

Fig 8
Times of manifestation

Material divided into 7 groups according to whether the persons were born before or after 1870. The times of manifestation are collected in decades. The object of this table is to find how many manifestations occur annually. The purpose of considering patients born after 1870 separately is to make it possible to compare with Fig. 1. It will be seen that 12-24 cases have occurred in each decade since 1910, i.e. one or two manifestations a year. The sum 12 of the last decade, however, is no doubt too low, as the study of several of the pedigrees was closed as early as 1964.

2 times of manifestation are lacking, as the time of manifestation in two males is not sufficiently well known to be placed in a 10-year group.

gård, a son of the proband's sister, became blind in 1939, but the cause of his blindness is unknown, as he was living in New York. At present the material comprises only 3 men born after 1913, but presumably this is sufficient for a decision to be made when the time comes as to whether or not an inherited predisposition exists in this family.

Fig. 40. The list of persons was partially reconstructed and supplemented by 1 person, 6 of whom were born after 1910. One new case occurred in 1943 in the proband's youngest sister. This case was mentioned by Lundsgård in a footnote. The pedigree comprises 13 persons born after 1919, still under observation.

Fig. 41. The list of persons in the two youngest generations has been recon-

	Males		Females	
	Observed	Affected	Observed	Affected
1860-69				
1870-79	12	10	21	4
1880-89	22	14	19	1
1890-99	39	21	33	6
1900-09	34	18	30	2
1910-19	36	14	35	4
1920-29	31	9	24	
1930-39	26	4	27	
1940-49	35	4	26	
1950-59	28	1	19	
sum	263	95	234	17

Fig 7

Number of persons born during each 10 year period. The reason why those born prior to 1870 have been omitted is that non affected persons from these years were estimated not to be fully represented in the register. It will be seen that among the persons born in the period 1870-1910 more than half the males have by now become affected.

Among the younger persons the affected persons as yet make up only a smaller proportion.

riod before 1960 which are unrelated to Lundsgård's pedigrees. Cf. also the following section on Lundsgård's "isolated cases".

Isolated Cases from the 1944 Study

Lundsgård's paper included another 7 pedigrees depicted in her thesis as Figs 39-45. These pedigrees will be mentioned in outline below without the detailed graphs.

Fig. 39. The list of persons has been reconstructed but the family has grown by only one boy born in 1953. With the exception of the line from one woman born in 1917 who could not be traced it has been found that the female lineage will become extinct. There is a great preponderance of undeterminable women in the generation under observation and the pedigree can give no conclusive answer to the question regarding the carrier rate. According to Lundsgård's

	Males			Females		
	Males born 1870	Males born 1871-1879	Males born 1880-1889	Females born 1870	Females born 1871-1879	Females born 1880-1889
1860-69		3	3		2	2
1870-79		3	3			
1880-89		8	8			
1890-99	7	6	13			
1900-09	7		7	3	1	4
1910-19	12	3	15	1		1
1920-29	10	1	11	4		4
1930-39	22		22	2		2
1940-49	8		8	5		5
1950-59	16		16	1		1
1960-69	11		11	1		1
total	93			17		

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Material divided into 2 groups according to whether the persons were born before or after 1870. The times of manifestation are collected in decades. The object of this table is to find how many manifestations occur annually. The purpose of considering patients born after 1870 separately is to make it possible to compare with Fig 1. It will be seen that 17-4 cases have occurred in each decade since 1910; i.e. one or two manifestations a year. The sum 17 of the last decade, however, is no doubt too low, as the study of several of the pedigrees was closed as early as 1964.

* Times of manifestation are lacking, as the time of manifestation in two males is not sufficiently well known to be placed in a 10-year group.

gård, a son of the proband's sister, became blind in 1939, but the cause of his blindness is unknown, as he was living in New York. At present the material comprises only 3 men born after 1910, but presumably this is sufficient for a decision to be made when the time comes as to whether or not an inherited predisposition exists in this family.

Fig 40. The list of persons was partially reconstructed and supplemented by persons 6 of whom were born after 1940. One new case occurred in 1943 in the proband's youngest sister. This case was mentioned by Lundsgård in a footnote. The pedigree comprises 13 persons born after 1919, still under observation.

Fig 41. The list of persons in the two youngest generations has been recon-

structed without new cases being found. There have been 7 male and 10 female cousins of the proband's—two of the males and one of the females living in America. As far as may be gathered from talks with a few of the family members, all are healthy, but the family is far from having been thoroughly investigated. Its members are very scattered. In particular, the emigration to America has had an inhibitory effect upon the initiative for investigation.

Fig. 42 This is an old pedigree. The proband was born in 1838. Lundsgård's knowledge of the family was based merely on studies of archives, and she never traced the connection to the present times. Nothing has been done to renew the knowledge of this family.

Fig. 43 The proband cannot be identified, and to day the persons are entirely unknown.

Fig. 44 The list of persons is known from an accidental remnant of Lundsgård's notes. The only female line is extinct, and this pedigree will never show more than it did in 1944.

Fig. 45 The pedigree has been supplemented by 28 persons, so that now it comprises 52, 31 of whom were born after 1900. There are 2 cases of optic atrophy among the male cousins of the proband's. Considering the predisposition, it is most likely that these are cases of Leber's disease. The diagnosis is in one of the cases: *Episodic psychosis in oligophrenia*, history of alcoholic abuse, toxic atrophy of both optic nerves. The disease arose in 1907, within one month after a bottle party on a ship in the docks; accordingly, his neuritis was interpreted as being toxic. The other cousin was admitted in 1958 to an eye department as a case of bilateral retrobulbar neuritis. Owing to a suspicion of suprasellar meningioma, exploratory craniotomy was performed. It showed a whitish, thickened arachnoid and yellowish optic nerves with a striking number of vessels above as well as below the chiasm, but no meningioma. These patients' next of kin have refused to supply information about the family, stating that the causes of blindness were alcohol abuse and brain disease respectively. Therefore, a study of this family is not really in progress, but it would afford a good material for observation.

Comments

The carrier rate in these pedigrees is at present no higher than 50%. The pedigrees containing isolated cases show, like the rest of the study, how families die out due to lacking reproduction in the female lineage, but they also give examples of how a case, which has once seemed isolated, is no longer isolated as time goes on. The last pedigree is of most interest, showing how one case in a family is so typical that it gives rise to a genetic study, while the next two in the same family may show a rather complicated disease pattern and do not give any impulse for genetic study.

DISCUSSION

Pedigrees A and C have become ideal. The women may be counted in two consecutive generations and in the next generations mothers are so numerous that a result may be expected when the next counting among women can be done. Pedigrees II E, F and H also fan out affording observation material but various factors reduce their value. Knowledge of family B is reduced by emigrations and by three alterations of the Danish German frontier since 1948. In pedigrees E, F and H only one generation of women is really suited for counting and the next generation now under observation (the 5th generation) comprises only 5 III and 2 mothers respectively. Pedigrees D and K include a relatively large number of childless women so that the youngest generations contain too few mothers for elucidating the mode of inheritance. The remainder of the pedigrees are characterized by female lines which are small or about to die out and by emigrations which obliterate the trace of the last persons that might be observed.

Within this heterogeneous material the findings in the ideal pedigrees A and C have maintained the presumption that the daughters of all carriers are carriers themselves because all mothers who have borne so many children that the inherited trait has had a possibility of manifesting itself have proved to be carriers. The question is then whether it is justified on this basis to feel convinced that the same applies to all families with Leber's disease.

The results of studying the other 18 pedigrees cannot disprove the presumption that all daughters of carriers are carriers themselves as the material does not contain women who can be labelled with certainty as non carriers. The existence of other families in which the disease occurs more scattered warns against drawing a general conclusion now although these families have been observed for only a short time. The fact that the Dutch material includes healthy branches should also urge to reserve. In my opinion therefore it is reasonable to demand a longer observation period so that new generations of satisfactorily observed mothers may be counted before general conclusions are drawn.

Considering that a number of the pedigrees embrace 4 generations and that the material includes cases occurring before Leber described the disease in 1811 it may seem surprising that there is still reason to demand a longer observation period to answer the question concerning the carrier rate. The question relating to the causes of lacking reproduction is incorporated in that relating to the carrier rate and is equally difficult to answer. Furthermore the observation makes the women aware of the indication for birth control and thereby observation might render it the more difficult to attain a result the more efforts are made to attain it.

It is apparent from the study that to be able to determine the carrier rate

one must have luck viz in finding the families that reproduce sufficiently. It has shown also that it is still necessary to establish knowledge of new families. If not we shall soon be left with a very small number of pedigrees.

It is unlikely that the mode of inheritance of Leber's disease could be a special one applying to this disease only. Better insight into the problems must be obtainable by comparison with pedigrees of other diseases transmitted through carriers. The reason why ophthalmologists have devoted so much interest to the mode of inheritance of Leber's disease is that a knowledge of the predisposition is required for differential diagnostic purposes. Collection of case histories by genetic studies has been needed to gain more knowledge of the pathognomy of the disease. Therefore the large pedigrees embracing many generations have been established and have given rise to the discussion on the carrier rate. If other diseases presented diagnostic difficulties which might necessitate the large pedigrees a few of them might perhaps also reveal a carrier rate so high that it could not be interpreted as being in accordance with the law of Mendel.

The advantage of the present material is that the pedigrees have been recorded as completely as at all possible and that apart from recording the women's descendants it is known also which of the women are childless and whether the latter have passed the entire fertile age. Those women who may have unknown descendants are marked by a special symbol and make up a minority. The time of onset of the disease is for each individual patient stated in the pedigree as suggested by Julia Bell originally with a view to studies of anticipation and the influence of external factors upon the mechanism of manifestation but here used as information necessary for the calculation of the manifestation rate. To keep this up the material must be reviewed about every 5 years. If 15 years are allowed to elapse the review will require too much work and some material will inevitably be lost.

The weak point of the material is that the majority of persons listed as healthy have not been examined ophthalmologically. As the domiciles are so scattered that one examiner is unable to supervise them all it would be practical to institute collaboration between the eye departments in the entire country and examine members of the families in the nearest department gradually as they reach the age of 60. Notification of new cases to a central register would also be of great value. Nation wide campaigns with the object of taking stock of the disease at 10 year intervals might inspire research.

Strictly statistical calculations were not done on this material as it is difficult to set up rules according to which it should be analysed. A satisfactory criterion of a non carrier has not been found. The more exacting this criterion in respect to number of descendants and observation period the more undetermined women will be found in the pedigree. Incidentally the pedigrees would have to be analysed separately because in the case of one pedigree there is

one reason and in the case of another a different reason why they are not ideal

The worker who collects a material of persons with Leber's hereditary optic neuritis is bound to write about the mode of inheritance because genetic studies are used in collecting the material. To bring research beyond this stage it is important thereafter to make the material accessible to the clinicians in their daily work so that the questions relating to the pathogenesis of the disease may arouse interest and be solved by a collaboration with pathologists, biochemists, physiologists and geneticists. It would be reasonable to try first to elucidate the question whether the optic atrophy in Leber's disease is ascending or descending. The high incidence of headache appears to indicate a cerebral disease. It would be desirable to demonstrate the anatomical basis of the disease but it is difficult for the pathologists to get material for study. The time of atrophy of the blood vessels in the disc does not give any decisive information about the seat of the primary lesion. Biopsy from the visual pathways in the acute stage is contra-indicated as it would harm the visual remnant. Post mortem examination of the brain is usually not done because at the time of death the eye disease is so old that it seems irrelevant. The similarity to the sequelae of alcohol poisoning suggests the association that the disease might be caused by a vulnerable enzyme system. The amblyopia which may complicate the treatment of depression with monoamine oxidase inhibitors (Emil Frandsen 1962) is very like Leber's optic neuritis. Studies on the pathogenesis of this visual damage might perhaps also throw some light upon the pathogenesis of Leber's optic neuritis. Investigations of the monoamine oxidase activity in the retina and optic nerve have been performed by several authors during the period after 1956 most recently by Anja Mustakallio in 1967.

The present material will afford help for the early diagnosis of the expected new cases of Leber's disease. The diagnosis may then be done immediately after the onset of the disease even during the unilateral stage. A few times doctors in these situations have felt that admission to hospital was unnecessary. However there are many reasons for admission. The patient is not up to being told the whole truth at once. Among other things he may react violently when learning that others have been aware of the predisposition without telling him about it. Remedies for migraine might be tested in the attempt to relieve the headache which may harass some of the patients for the remainder of their lives. The significance of physical exertion during the stage of neuritis to the visual end result has not been fully elucidated. In cases where the disease starts on one side only it might be investigated in future whether the end result in the latter eye is better if the patient is spared physical exertion during the stage of neuritis. This question must be settled before the early diagnosis perhaps results in the patients being made to work or is started on too early a training in an occupation for the blind.

It is a fact that a number of the cases reported in the present study would not have been diagnosed as Leber's disease if this review of the pedigrees had not been carried out. As a matter of course it is difficult to determine the centre of a central scotoma. Indeed, a review of the case records shows that examination of the same patient at different times or by different examiners may result in different locations of the scotoma with centre in the visual axis, centrocoecal, quadrantic or hemianopic. It must be admitted that the clinician is faced with this difficulty and to consider the diagnosis of Leber's disease when ever coming across a scotoma involving the central part of the visual field. Fixation ring on the perimeter as described by *Weve* (1942) and modified by *van Senus* (1963) is to be recommended. If a patient with Leber's optic neuritis is subjected to exploratory craniotomy because the inherited predisposition is unknown and there is a suspicion of a juxtachiasmal lesion it is of course regrettable that the patient has to submit to an operation which has no therapeutic effect but it must be considered a reasonable step in the given situation. It is maybe more unfortunate for the patient if his condition is diagnosed as alcohol amblyopia. An alcoholic among patients with Leber's disease is in a very bad position. His financial situation as well as his marriage may break up and the visual loss is great. The patient is lonely and alone because his eye disease is interpreted as self inflicted. The diagnosis of alcohol amblyopia will be entered on his papers in the public assistance office and disablement insurance court and will not be forgotten even though an inherited predisposition is demonstrated later.

Still we have a possibility of getting nearer to the problems relating to Leber's disease by carefully noting all features of its acute stage and procuring accurate knowledge about its prevalence but presumably the desired results can be attained only by direct collaboration between geneticists and biochemists in elucidating the mode of inheritance as well as the mechanism of manifestation.

Conclusion

In two out of 20 pedigrees both followed through 8 generations and representing 229 and 116 persons respectively it was not possible to demonstrate mothers who could be said with certainty to be free of the trait. The results of studying these two pedigrees support the assumption that all women born in the pure female lineage are carriers. This result cannot be disproved by the study of the other 18 pedigrees. Thus the study has demonstrated that a carrier rate of 100% does occur. It has made probable but not definitely proven that this is a general rule.

References

- Bell Julia* Hereditary optic atrophy *The treasury of Inheritance* 2 (1931) 4
- Frandsen E* Toksik Amblyopi ved Behandling med Antidepressiva *Ugeskr Læger* 124 (1962) 18 610
- von Goethe J W* Die Schriften zur Naturwissenschaft. Physische Farben. Älteste aufmunternde Teilnahme. I (1962) 4 215 270
- Lundsgård Ruth* Lebers Disease *Acta Ophth suppl* 21 Thesis 1944
- Mustakallio Anja* Monoamine Oxidase Activity in the various structures of the Mamalian Eye *Acta Ophth. suppl* 93 Thesis 1967
- Quattlebaum Jul K* Stroke Associated with Elongation and Binking of the Internal Carotid Artery *Annals of Surgery* 120 (1929) 874
- Scedorff Tove* Lebers Disease *Acta Ophth* 46 (1968) 4
- Scedorff Tove* Lebers Disease II *Acta Ophth* 46 (1968) 935
- Scedorff Tove* Lebers Disease III *Acta Ophth* 47 (1969) 23
- Scedorff Tove* Lebers Disease IV *Acta Ophth* 47 (1969) 813
- van Senus A H C* Lebers Disease in the Netherlands Gravenhage 1963 Thesis
- Wetzel H J M* 1947 quoted from van Senus

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DENDRITIC (HERPETIC) KERATITIS

II Follow Up Examination of Corneal Opacity (Opacity vascularisation Hudson Stahli's line sequelae of iritis)

BY

M S NORN

Cicatrization is often seen in the cornea as a persistent sequela of dendritic keratitis. Will such cicatrization abate in the course of time? or is it more likely to exacerbate owing to further relapses? Has the chance of cicatrization become reduced after introduction of 5 iodo 2 -deoxyuridine (IDU) treatment and which is the course in patients previously treated with steroids?

These are some of the questions that are of current interest because the disease is so relatively common and because several therapeutic possibilities exist including corneal transplantation.

The study reported below comprised 109 patients followed up on an average 13 years after their first attack of dendritic keratitis.

The composition of the material age and sex incidence, recurrence rate and visual acuity at the follow up have been reviewed in a previous paper (Norn 1969).

It was pointed out that the series of patients was selected consisting solely of such as had been referred to an ophthalmologic unit for out patient treatment whereas not the great number treated by ophthalmic medical practitioners.

The series must therefore be supposed to comprise the fairly grave cases of herpetic keratitis.

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Corneal Opacity

The report includes 107 patients with previous attacks of dendritic keratitis two having been ruled out owing to corneal transplantation

All the follow up examinations were carried out by the author

The degree of opacity was estimated in the slit lamp also at subdued light in the room (slit lamp in darkroom) and by scleral scatter (intense slit lamp rays against the sclera at the limbus observation of the cornea through the slit lamp ocular and with the naked eye) thereby to disclose even the slightest opacity of the cornea

The area form and depth of the opacity have been entered in a diagram sketching the frontal and sagittal planes

Incidence and Site

Corneal opacity was detected in 91 cases (85 per cent) A sequela of keratitis is thus demonstrable in most cases even long after the attack

This result is in agreement with Thygeson's statement Scar formation is a principal if not invariable sequela of all corneal disease due to herpes simplex virus (1957)

The opacity was in most cases localized centrally covering the pupillary area When situated excentrically as was rarer it was most often found temporally (fig 1)

Morphology

In a great number of the eyes (44 per cent) an uncharacteristic, more or less

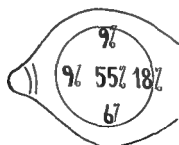


Fig 1

Localization of the opacity in 91 patients who had had dendritic keratitis. Percentage distribution. In 4 per cent the opacity extended obliquely from one limbus to the opposite one.

disc shaped opacity was seen. This was in some cases rather irregularly outlined, sometimes having off shoots which rarely were ramified.

In 21 per cent there were found two or more disc formed opacities and in 10 per cent one or more punctate opacities.

Only one fourth (25 per cent) of the patients showed opacities so characteristic that their appearance raised suspicion of previous dendritic keratitis. Round opacities connected by off shoots were found and occasionally ramified opacities of the same shape as the typical dendritic keratitis pattern though somewhat broader.

Transitional forms between the types described above were also seen.

Area of Corneal opacity

The extension of the opacity in the frontal plane was sketched in a diagram and on the basis of this its size was roughly referred to one of the following categories, set up by *Mackenzie*:

1) pinpoint size 2) less than 3 mm in diameter 3) less than one sixteenth of the corneal area 4) less than one eighth 5) less than one fourth 6) less than half 7) more than half of the total area of the cornea

The opacity covered on an average about 10 per cent of the corneal surface. More than half of the cornea was covered in no more than 3 per cent and between one half and one fourth in 4 per cent (table I).

As might be expected there was no complete correlation between the area of the opacity and the *visual impairment* among other things because the site in relation to the centre is of decisive importance.

Thus a patient with an opacity covering less than one fourth of the corneal area had a vision of only 6/36 while another had 6/6 with an opacity covering more than one fourth of the cornea.

In table I the series has been divided into groups according to the *length of the observation period*. The table shows that the opacity generally was the largest in the series with the longest observation period being on an average twice the size of that in the group observed for a short period.

There were in other words no positive signs that an opacity may decrease in the course of time.

The opacity increased in size with *rising number of attacks*. The opaque area was on an average more than doubled in the group with over three attacks compared with that in the group with only one attack.

One patient completely avoided development of an opacity despite ten attacks.

The opaque area was seen to be independent of the patient's sex and of the age at first attack.

The series has been divided into three groups on the basis of the therapy.

instituted (steroid IDU or iodine cauterisation) Patients given more than one form of treatment have been counted in the corresponding groups The series would become too small if it were to include solely the patients given only one form of treatment

It is seen in the table that the area of the opacity generally was the largest in the patients treated with *steroids* This may be due to the fact that steroids were only given to patients whose disease had grown worse with impending or established metaherpetic development and who therefore were liable to more extensive opacity Steroids were administered in the hope of reducing corneal oedema and preventing further corneal opacity The final result was poorer than in the non steroid treated cases

The *IDU treated* and the *iodine cauterized* cases showed opacities approximately equal in size We must bear in mind however that the average observation period was considerably shorter for the IDU treated than for the others (Vorn 1969) As moreover the recurrence rate seemed to be higher among the IDU treated these might be feared to get more extensive opacities in the course of time than the iodine cauterized

Depth of Corneal Opacity

The depth of the opacity has been roughly characterized as follows

I) thin II) less than one fourth of the total corneal depth III) less than half IV) less than three fourths and V) more than three fourths of the total corneal depth (table I)

No correlation was noticed between the depth of the opacity and the visual impairment Of two patients both with an opacity so thick as to comprise more than three fourths of the cornea in depth one had 6/6 and the other 6/36

In the majority the opacity comprised only the most superficial portion of the corneal stroma In one case it was most intense in the deep layers while in eleven cases there was both superficial and deep condensation with a clearer zone in between and in three cases more irregular opaque bands in the stroma

In a small number of cases the cornea was definitely thinner at the site of the opacity with less anterior corneal curving

The opacity was relatively deep in patients observed for a long period and patients having had several relapses Further it was deeper after steroid treatment than after IDU treatment and cauterisation in which latter groups it was on an average of the same depth

Vascularisation

The blood vessel invasion of the cornea has been graded as follows

A) minimal invasion B) invasion 1-3 mm from the limbus C) invasion of about half of the corneal area D) invasion comprising almost the entire corneal area

Blood vessel invasion was seen in half of all the eyes. Blood vessel invasion without associated opacity was observed in one case only, while 39 presented opacity without blood vessel invasion.

The vascularisation tended to be most pronounced in the cases with the largest opacity (in area and depth) (table I).

A granular blood stream was in nearly all the cases seen to flow through the vessels invading the cornea. Only few vessels showed no blood stream whatever (ghost vessels).

The vascularisation was on an average most pronounced in the patients observed for a long period and patients who had had many attacks compared with those who had had few or only one attack. 28 out of 43 patients with only one attack were free from blood vessel invasion against no more than 8 out of 23 after three attacks.

The possible influence of the treatment on blood vessel invasion is shown in table II. No significant difference was found between the IDU treated, the iodine cauterized and the total series.

The observation period was as stated the shortest for the IDU treated. Hence vascularisation must be feared to follow renewed relapses.

One of the reasons for giving steroid was that of reducing the corneal oedema which constitutes a contributory factor in blood vessel invasion. Nevertheless definitely increased vascularisation was found in the steroid treated group.

Half of the total series had had a herpetic eruption on the lips at some time or other.

No correlation was demonstrated between previous herpes of the lips on one hand and vascularisation of the cornea and the area or depth of the opacity on the other.

Hudson-Stahl's Line

Hudson-Stahl's line is a thin brownish line which when typical runs a horizontal course under the centre of the cornea between the upper two thirds and the lower one third of the cornea.

The line may be found in normals in steadily increasing numbers with maximum in the age class of 60-69. After the age of 70 the frequency falls again (Norn 1968 A) (table III).

Hudson-Stahl's line was much more frequent in this series than among normals being present in 52 per cent of all who had had dendritic keratitis. The

Table I

Size of opacity after dendritic keratitis dependence on observation period number of relapses therapy (steroid IDU or iodine cauterisation) Possible correlation of vascularisation with opacity 107 patients

The figures in the table indicate the number of patient except within the therapy survey where the figures represent percentage of treated in the group concerned

Grading of opacity area

1) pinpoint size 2) < 3 mm in diameter 3) < $\frac{1}{16}$ of the corneal area 4) < $\frac{1}{8}$ 5) < $\frac{1}{4}$ 6) < $\frac{1}{2}$ 7) > $\frac{1}{2}$ of the corneal area.

Grading of opacity depth

I) thin II) < $\frac{1}{4}$ of the total corneal depth III) < $\frac{1}{2}$ IV) < $\frac{3}{4}$ V) > $\frac{3}{4}$ of the total corneal depth

Grading of vascularisation

A) minimal B) extending 1-2 mm inwards from the limbus C) covering about half of the cornea, D) covering almost the whole cornea

	opacity area								mean area	opacity depth					
	0	I	2	3	4	5	6	7		I	II	III	IV	V	Total
obs period															
< 8 yrs	7	3	12	4	6	4	0	1	0.04	16	9	1	0	4	37
9-1 yrs	8	0	13	7	6	4	3	0	0.090	15	10	3	1	4	41
> 15 yrs	1	1	4	5	8	7	1	2	0.174	8	5	2	3	10	29
number of attacks															
1	14	3	13	3	4	4	1	1	0.063	15	7	3	0	4	43
2-3	1	0	15	9	7	6	7	1	0.114	20	11	1	7	6	41
> 4	1	1	1	4	9	5	1	1	0.165	4	6	2	2	8	23
therapy (n per cent of treated in the group concerned)															
steroid	6	0	7	10	25	22	3	3	0.134	25	25	6	8	31	36
IDU	11	4	31	9	26	13	2	4	0.108	35	31	6	4	15	34
iodine cauterisation															
total	15		5	19	21	15	3	1	0.115	37	1	11	4	16	81
total	15	4	7	15	11	14	4	3	0.10	36	27	6	4	17	107
vascularisation															
A	15	4	19		5	1	0	0		25	11	3	0	11	54
B	0	0	6	1	1	1	0	0		5	2	1	11	1	9
C	1	0	4	11	11	5	1	2		9	9		1	8	30
D	0	0	0	1	0	5	7	0		0	2	0		4	8
	0	0	0	1	0	3	1	1		0	0	0	1	5	11

Table II

Blood vessel invasion of the cornea dependence on therapy

The figures indicate in per cent the degree of vascularisation within the therapy group concerned

The degrees of vascularisation indicated by A D as in table I

vascularisation	0	A	B	C	D	Total
IDU	56	4	30	4	7	54
steroid	31	8	36	14	11	36
iodine						
cauterisation	47	10	28	10	5	81
Total	50	8	28	7	6	107

incidence being fairly independent of age the rising frequency with increasing years among normals was masked in this pathological series

The line was more frequently present in the pathological eye than in the contralateral (table III)

The distinctness of the line was roughly graded 1 to 5 (grade 1 being a very weak only just recognizable line grade 3 a moderately pronounced line and grade 5 a maximally pronounced line An identical grading was employed by the author in the normal series)

In the young age classes of the normal series the grade of Stahl's line when this was present at all averaged 1.0 and in the older age classes maximally 1.6

In the present pathological series with previous dendritic keratitis the line was on an average of grade 2.4 apparently independent of age Stahl's line was in other words much more pronounced than in the normal series and more than in the contralateral eye where the average was 1.4

Summarizing we may conclude that Stahl's line is much more frequent and more pronounced in patients who have previously had dendritic keratitis than in normals

Stahl's line hardly bears any direct relation to corneal opacity since cases were found showing opacity but not Stahl's line (39) and others showing Stahl's line but no opacity (4)

Stahl's line tends perhaps to occur more frequently and be more distinct in cases with a fairly extensive and deep opacity as well as vascularisation of the cornea

Of the patients with blood vessel invasion 59 per cent had Stahl's line against 41 per cent of those without vascularisation

Table III
Incidence of Stahli's line among 100 patients who had had dendritic keratitis Incidence in the contralateral eye compared with that in a
in selected clinical series (700 patients)

age	per cent with Stahli's line			mean degr of Stahli's line		number of patients dendr
	seq of dendr keratitis	contralat	normal series	dendr	control	
<10	50	18	0	23	10	27
10-19	42	20	2	14	10	11
20-29	6	0	11	29	0	13
30-39	25	33	14	47	10	12
40-49	60	58	22	25	13	20
50-59	47	50	31	24	20	17
60-69	73	63	44	20	16	11

Stahl's line was often seen to lie close to or within the region of a corneal opacity

Bizarre forms of Stahl's line were often seen two lines situated one above the other or beside each other a completely irregular serpentine line a Y shaped line a line having the form of a lying H and a horizontal line in the upper one third of the cornea Similar bizarre forms were however also met with in the normal series

Posterior Surface of Cornea

Folds of Descemet's membrane were found in four cases and a pigmented double line on the posterior corneal surface in one probably due to rupture of Descemet's membrane

In one case pigment flakes were seen on the posterior corneal surface

In seven cases residual precipitates were seen scattered on the posterior corneal surface Such were not observed in the contralateral normal eye

Aqueous flare was found in one case only in which the cornea was also stained by rose bengal suggesting active dendritic keratitis

Iris

In one case synechiae were seen between the iris and the lens and in one connective tissue membrane across the pupil as a sign of previous iritis

All the 107 patients were examined for iris transparency according to *Abrams*

In darkroom the patient fixes the light of the slit lamp (Haag Streit slit lamp No 900) The width of the slit is adjusted to just under the size of the pupil the axes of light and ocular are made to coincide and focusing is performed corresponding to the posterior surface of the iris The pupil will then reflect a red light as will also defects of the pigmentary layer of the iris Holes as small as $10-20\mu$ corresponding to disappearance of a single cell are recognizable Different visual angles are employed to avoid disturbing corneal reflex (*Abrams Norn 1968 C*)

Examination using *Abrams*' technique revealed defects of the pigmentary layer of the iris in 22 patients

Three were found to have fairly large local round or oval defects in the pig

mentary layer between the pupil and the periphery. The defects were similar to such as may be found after iritis.

One had a well defined sector formed defect and one a flat irregular defect likewise covering most of a sector.

Four had defects in the pupillary border of the affected eye whereas not in that of the contralateral eye.

Thus altogether nine patients displayed defects of the pigmentary layer of the iris which presumably were due to iritis caused by herpes virus.

In two cases pigmentary defects were seen following antiglaucomatous operation (iridectomy iridencleisis).

Pupillary border defects alike in the two eyes were found in seven cases while in four cases fine punctate defects were fairly equally present inferiorly in the iris of both eyes. These defects must be regarded as physiological.

Signs of previous iritis were found in 22 of the 107 dendritic keratitis patients (characteristic iris defects synechiae precipitates etc). Active iritis was suspected in one case only.

No case was referable to the steroid induced chronic kerato uveitis.

Nearly half of the steroid treated patients of the present series belonged to the group with signs of previous iritis while only one fifth of the iodine cauterized and one sixth of the IDU treated displayed such signs.

Corneal Transplantation

Two patients had had corneal transplantation performed one with a favourable result (vision 6/12 owing to immature cataract). In the other case the transplantation was complicated by recurrence of dendritic keratitis in the graft with consequent clouding (vision 6/36).

It has been found reasonable to consider corneal transplantation in 18 of the 10 cases in which the vision was under 6/18.

However in three cases operation was not advised. One patient had the first attack of keratitis as early as the age of 4.5 and the eye is possibly amblyopic one was found unfit for psychic reasons and one for social (alcoholic).

Four had previously been interested in corneal transplantation but they had now become so used to the impaired vision of one eye that they no longer desired operation.

Ten patients were not interested in corneal transplantation because they managed well visually with the healthy eye.

One desired operation (1/4 of both eyes).

Thus only three out of 109 patients with previously diagnosed dendritic keratitis had been subjected to or desired corneal transplantation.

Stahl's line was often seen to lie close to or within the region of a corneal opacity

Bizarre forms of Stahl's line were often seen two lines situated one above the other or beside each other a completely irregular serpentine line a Y shaped line a line having the form of a lying H and a horizontal line in the upper one third of the cornea Similar bizarre forms were however also met with in the normal series

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Three were found to have fairly large local round or oval defects in the pig

The size of the opacity and the degree of vascularisation might therefore be conceived to be the least alarming for the patients treated by iodine cauterisation alone

Hudson Stahl's line is more frequent and more pronounced among patients who have had dendritic keratitis than among normals. The difference is particularly significant in the young age groups where the line is rarely seen in normals.

I concluded on the basis of a pathological series comprising 364 patients that the line is relatively frequent in association with uveitis in particular anterior uveitis and that the line may bear relation to a corneal cicatrix in extremely few cases only (Vorn 1968 B)

The frequent occurrence of Hudson Stahl's line after dendritic keratitis is perhaps in part explainable by the high incidences of corneal opacity and iritis in this series. On the other hand other factors bearing relation to the herpes virus may also have played a role. The cause of Stahl's line is still obscure.

Only 2 per cent of the total series have been subjected to corneal transplantation and only few of the others are likely to have this operation performed. This low number in spite of many grave cases is due to a hesitating attitude towards transplantation among patients whose contralateral eye is intact.

In a future paper the results will be reported of examinations concentrating on the precorneal film vital staining and Fischer-Schweitzer's polygonal fluorescein pattern carried out on the present series. The object of these examinations have been to clarify if possible, whether such investigations into the superficial pathology of the cornea can yield further details of clinical value in the control of patients having had dendritic keratitis.

Summary

A series of 109 patients who had had dendritic keratitis (the first attack on an average 15 years previously) have been followed up.

Corneal opacity was seen in 85 per cent most often localized centrally. It was ramified in no more than one fourth of the cases and covered on an average 10 per cent of the corneal area.

Blood vessel invasion was found in half of the affected eyes.

The size of the opacity (area and depth) and the vascularisation were seen to become aggravated with increasing length of the observation period as well as after some relapses after treatment with steroids and probably also after IDU treatment.

The result of the present investigation suggested that iodine cauterisation gives the least opacity.

Local Tanderil Treatment

In an attempt to reduce the corneal opacity I treated 18 of the most gravely affected eyes with *oxiphenbutazonum* NFN (tanderil Geigy ointment 10 %) an anti inflammatory agent hydroxyphenylbutazone)

In one case recurrence of dendritic keratitis was noticed before the treatment and in five punctate staining (fluorescein or rose bengal) prior to the treatment. The remainder showed no signs whatever of activity on prescription of the ointment.

This therapy was not followed by activation of the dendritic keratitis. On the other hand no improvement was seen either presumably because the treatment was instituted too late.

Application of tanderil at the active stage has not been tried.

Such investigations are under preparation (Geigy's workshop on ophthalmology in Kandersteg jan 1970).

Discussion

The series under review was in some measure selected constituting fairly grave cases of dendritic keratitis. This may possibly account for the fact that sequelae of previous iritis were seen in so many patients (21 per cent).

The prognosis of dendritic keratitis is poor. In particular the condition has been found to deteriorate with increasing length of the observation period owing to frequent relapses while conversely signs of spontaneous clearing up of the cornea have never been observed. The longer the observation period the more does the opacity grow in area and depth with associated increasing vascularisation.

The visual impairment has been shown previously to be the greatest after steroid treatment (Norn 1969). In the present series this group was found to be burdened with a larger opacity area and depth, a more intense vascularisation and more frequent signs of iritis than the other groups.

As pointed out above these phenomena might all theoretically be accountable for by the fact that steroid is preferably administered to the severest cases in which the prognosis already is particularly poor. However Thygeson (1967) has shown that steroid is contraindicated in cases of dendritic keratitis.

As for IDU treatment the degree of visual impairment, the size of the opacity and the degree of vascularisation seemed to be independent of the treatment. However the average observation period was shorter for this group than for the remaining series. It is therefore to be feared that further relapses may render the final result poorer than that for the patients not given IDU.

The size of the opacity and the degree of vascularisation might therefore be conceived to be the least alarming for the patients treated by iodine cauterisation alone

Hudson Stahl's line is more frequent and more pronounced among patients who have had dendritic keratitis than among normals. The difference is particularly significant in the young age groups where the line is rarely seen in normals.

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Blood vessel invasion was found in half of the affected eyes.

The size of the opacity (area and depth) and the vascularisation were seen to become aggravated with increasing length of the observation period, as well as after some relapses after treatment with steroids and probably also after IDU treatment.

The result of the present investigation suggested that iodine cauterisation gives the least opacity.

Hudson Stahl's line was found in 52 per cent apparently equally often in the different age groups and more frequently than in a normal series where the line is a fairly rare phenomenon especially in the young age classes

Signs of previous iritis were seen in 21 per cent (defects of the pigmentary layer of the iris synechiae precipitates etc)

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References

- Abrams J D Transillumination of the iris during routine slit lamp examination Brit J Ophthal 48 42 45 (1964)
- Mackenzie A D A comparison of IDU solution IDU ointment and carbolization in the treatment of dendritic corneal ulcer Brit J Ophthal 48 214 216 (1964)
- Maumenee Edward Herpes simplex iridocyclitis In Aronson et al Clinical methods in uveitis Mosby S Louis (1968)
- Norn M S Hudson Stahl's line of cornea I Incidence and morphology Acta Ophthal 46 106 118 (1968 A)
- Norn M S Hudson Stahl's line of cornea II Aetiological studies Acta Ophthal 46 119 128 (1968 B)
- Norn M S Can defects in the iris pigment layers regenerate? Acta Ophthal 46 243 253 (1968 C)
- Norn M S Dendritic (herpetic) keratitis I Incidence seasonal variations recurrence rate visual impairment therapy Acta Ophthal 48 91 101 (1970 C)
- Thygeson Ph & Samuel J Kimura Deep forms of herpetic keratitis Am J Ophthal 43 part II 109 113 (1957)
- Thygeson Phillips Chronic herpetic keratouveitis Trans Am Ophthal Soc 65 211 226 (1967)

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DENDRITIC (HERPETIC) KERATITIS
III Follow up Examination of the Precorneal Film
Fischer Schweitzer's Fluorescein Pattern
and Vital Staining

BY

M S NORN

Dendritic keratitis is an often painful disease which frequently recurs

The author of the present paper summoned 104 patients who had previously had herpetic keratitis to a follow up partly to see whether any of these patients presented recurrence recognized or symptom free at the follow up and partly to make out how often sequelae of keratitis are detectable in the forms of corneal cicatrices blood vessel invasion impaired vision etc

The selection and composition of the series as well as the recurrence rate observation periods opacity vascularisation Hudson Stahli's line and visual impairment have been described in previous papers (Norn 1969 C and D)

In the present paper an account is given of the result of vital staining at the follow up Two vital stains were used (fluorescein and rose bengal) At the same time I took the opportunity of examining the vital stained precorneal film further I massaged the eyelid for the purpose of eliciting the fluorescein stained corneal mosaic pattern which is seen in normals but is absent in the presence of pathological processes in the superficial part of the cornea

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Wetting time

The precorneal film is the thin fluid layer covering the cornea (*N Ehlers*)

The precorneal film is the thickest immediately after blinking. It then grows increasingly thinner finally to burst. A hole is formed which is most plainly visible in the fluorescein stained precorneal film when this is observed in the slit lamp with cobalt-filtered light.

The wetting time means the interval from the conclusion of blinking to the start of hole formation in the precorneal film.

On examining a *normal series* with fluorescein stained precorneal film I found a mean wetting time of 30 seconds.

The wetting time was independent of addition of 0.3% oxibuprocaine chlor NFN (Novesin Wander) (*Norn 1969 A*).

For the present follow up of patients with previously diagnosed dendritic keratitis the same technique was employed as for the above mentioned examination of a normal series.

The patient is placed in front of the slit lamp. 0.125% fluorescein with 0.3% novesin added is instilled. The patient blinks twice or more. The precorneal film is observed in the cobalt filtered light of the slit lamp and the time elapsing until hole formation is first visible is measured using a stop watch.

The patient is requested to keep the eye open voluntarily during the examination. The lids are not supported by the examiner.

A total of 107 patients who had had dendritic keratitis were examined. The mean wetting time was 17 seconds or considerably shorter than that in a normal series where using the same technique I found it to be 30 seconds.

Even though most of the patients no longer had active keratitis (see later) many were found to have a pathological reduced wetting time.

In the present series there was no sex difference (45 women had a wetting time averaging 18 seconds and 62 men 16 seconds).

In this respect the series thus differs from the normal series where the wetting time was considerably shorter for women than for men (24 against 36 seconds).

The normal longer wetting time for men becomes reduced or even eliminated in a pathological series where both sexes have a reduced wetting time.

The shorter wetting time in patients who have had dendritic keratitis might be due to the frequent occurrence of an opacity which must be supposed to constitute a poor foundation of the precorneal film.

Table I shows however that the wetting time also was reduced in the cases where no opacity was detectable (averaging 20 seconds).

The wetting time is perhaps the shortest in the cases with the deepest opacity whereas the area seems to have no influence.

In cases with corneal opacity from other causes no pathological wetting time was demonstrable (Norn 1969 A)

Permanent Holes in the Precorneal Film

Permanent holes in the precorneal film are such as are recognized immediately on concluded blinking. These holes are seen at the same site on re examination unlike the holes occurring after a certain interval.

Permanent holes (wetting time zero) are only found in pathological cases (Norn 1969 B).

In the present series permanent holes were found in 15 per cent of the 107 examined and only in cases with corneal opacity.

In five cases the dry spot in the precorneal film was noticed at the site of a small fluorescein stained erosion or keratitis while in two it was due to a visible small epithelial vesicle and in one to corneal oedema.

Two patients presented a rose bengal stained area at the site of the dry spot and one a calcareous spot in the opacity.

Thus in eight cases a reasonable pathological explanation could be given of the permanent hole formation in the precorneal film: a corneal defect (erosion, keratitis) or a vesicle on the cornea. In another three cases there was a possible explanation.

In the remaining five cases the dry spot was likewise seen over an opacity.

Table 1

Table dependence of the wetting time on the depth and area of the opacity 107 patients who had had dendritic keratitis

Opacity depth	Wetting time	No. of pts	Opacity area	Wetting time	No. of pts
no opacity	0	16	no opacity	20	16
thin	0	39	< 3 mm	21	33
< 1/4	1	4	< 1/16	11	16
<	3	6	< 1/8	13	0
< 5/4	11	4	< 1/4	10	15
> 5/4	14	19	> 1/4	23	7
Total	17	10		1	10

in four cases at the site of a peripheral sparing in Fischer Schweitzer's pattern and in one at a corresponding central sparing (see later)

In these cases the dry spot in the precorneal film must also be supposed to be accountable for by a pathological process which however is not detectable otherwise than by a permanent hole formation in the precorneal film remaining at the same site on repeated examination

The permanent hole formation can thus give additional information on the pathology of the cornea of patients with previous attacks of dendritic keratitis On the other hand this pathological condition is only disclosed in the cases with presence of corneal opacity No instance has been found of a permanently dry hole in an otherwise normal cornea

The permanent hole formation and wetting time seem to be independent of the therapy given though with a tendency to most pronounced pathological values among the steroid treated

The mean wetting time in the steroid treated series was 14 seconds in the IDU treated 19 seconds and in the iodine cauterized 16 seconds while in the total series it was 17 seconds

Fischer-Schweitzer's Polygonal Pattern

Fischer demonstrated in 1928 that by rubbing the cornea through the closed lid a net like pattern could be provoked in strong light reflected from the cornea on a screen

Schweitzer showed that the same net like pattern can be produced without use of any special apparatus by rubbing the cornea after instillation of 0.2% fluorescein into the conjunctival sac The pattern can be studied in cobalt filtered light in the slit lamp

The pattern is always present in normals but absent over a corneal opacity or nubecula and occasionally also in cases of corneal oedema and erosion

The pattern has been described later in relation to clinical series by Brown and by Norm (1968) in the latter paper named Schweitzer's pattern

Schweitzer has remarked to this (personal communication) that I would strongly suggest that this pattern should be called after Fischer who taught me ophthalmology when I was a student If any work was fundamental it was his

The term Fischer-Schweitzer's pattern has therefore been preferred in this paper

Examination for Fischer-Schweitzer's fluorescein pattern was carried out as follows

0.125% fluorescein with 0.3% novesin added was instilled into the conjunctival sac The patient was placed in front of the slit lamp The cornea was

massaged gently and rapidly with the examiner's finger on the closed lid. The cornea was examined immediately after in cobalt filtered light in a Haag Streit slit lamp No 900.

If a mosaic pattern was not seen or was indistinct the massage and the examination were repeated if necessary after renewed staining with fluorescein or with a mixture of 1% fluorescein and 1% rose bengal.

Result

Fischer-Schweitzer's pattern was pathological in most of the examined patients (19 per cent) who had had dendritic keratitis.

The pattern was totally absent in eight of the 107 examined even after repeated examination while it was normal in the contralateral eye (table II).

In the remaining cases more or less of the fluorescein pattern was absent. There were found one or more rather central areas with no pattern surrounded by normal pattern (fig. 1) or a peripheral sparing (fig. 2) or the fluorescein pattern was so greatly reduced that only one or more islets were seen on an otherwise pattern free cornea.

The sparing of the pattern often corresponded to a corneal opacity. In some instances it covered exactly the same area as the opacity (fig. 1) while in others it was a little smaller or larger than the opacity.

However cases may be found with a normal Fischer-Schweitzer's pattern despite presence of a distinct opacity. This was so in 12 patients (six punctate or small thin opacities, five fairly large central opacities extending through at

Table II
Pathological Fischer-Schweitzer's fluorescein pattern in 107 patients with previous dendritic keratitis

	number of patients
totally absent	8
residual islet(s)	31
one central sparing	72
two or more central sparing	10
peripheral sparing	10
central and peripheral sparing	3
Total number with pathological Fischer-Schweitzer's fluorescein pattern	84

in four cases at the site of a peripheral sparing in Fischer Schweitzer's pattern and in one at a corresponding central sparing (see later)

In these cases the dry spot in the precorneal film must also be supposed to be accountable for by a pathological process which, however, is not detectable otherwise than by a permanent hole formation in the precorneal film remaining at the same site on repeated examination

The permanent hole formation can thus give additional information on the pathology of the cornea of patients with previous attacks of dendritic keratitis On the other hand this pathological condition is only disclosed in the case with presence of corneal opacity No instance has been found of a permanent dry hole in an otherwise normal cornea

The permanent hole formation and wetting-time seem to be independent of the therapy given though with a tendency to most pronounced pathological values among the steroid treated

The mean wetting time in the steroid treated series was 14 seconds in the IDU treated 19 seconds and in the iodine cauterized 16 seconds while in the total series it was 17 seconds

Fischer-Schweitzer's Polygonal Pattern

Fischer demonstrated in 1928 that by rubbing the cornea through the closed lid a net like pattern could be provoked in strong light reflected from the cornea on a screen

Schweitzer showed that the same net like pattern can be produced without use of any special apparatus by rubbing the cornea after instillation of 0.2% fluorescein into the conjunctival sac The pattern can be studied in cobalt filtered light in the slit lamp

The pattern is always present in normals but absent over a corneal opacity or nubecula and occasionally also in cases of corneal oedema and erosion

The pattern has been described later in relation to clinical series by Bron and by Norm (1968) in the latter paper named Schweitzer's pattern

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In two of these cases Fischer Schweitzer's pattern was totally absent (normal pattern contralaterally)

Two showed sparing of the pattern inferiorly at the site of a previous dendritic keratitis as seen in the case record

In one case two islets were seen nasally in the pattern at the site of previous keratitis (fig 3)

Fischer Schweitzer's technique thus serves as evidence - even in some cases without opacity - not only that a patient has had keratitis but also where this was located

The method is therefore suitable as a supplementary test in cases where it is desired to know whether a patient may have had dendritic keratitis e.g. before instituting local steroid treatment or when examining a potential contact lens wearer

However of the 107 patients included in this study eleven (10 per cent) displayed neither opacity nor an abnormal Fischer Schweitzer's pattern

An only doubtful correlation was noticed between the treatment given and a pathological Fischer Schweitzer's pattern (92 per cent of the steroid treated 83 per cent of the IDU treated and 19 per cent of the iodine cauterized had a pathological pattern)

Vital Staining

Vital staining was performed by instillation of 0.01 ml of a mixture containing 1% fluorescein and 1% rose bengal (Norm 1964)

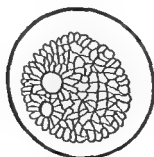


Fig 3

A man had a typical dendritic keratitis nasally of the left eye at the age of 34. At a follow up 11 years later the cornea seemed to be normal (no opacity nor nubecula, not at scleral scatter either no vascularisation nor Hudson Stahli's line, corneal sensitivity normal)

Fischer Schweitzer's fluorescein pattern showed two distinct defects at the site of the previous keratitis

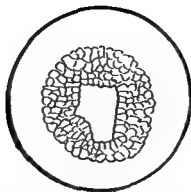


Fig 1

A woman had dendritic keratitis at the age of 23. No recurrence. A follow up 7 years later revealed superficial opacity and central sparing of a pronounced *Fischer Schweitzer's* fluorescein pattern corresponding exactly in area and shape to the opacity.

most one half of the corneal depth and one peripheral opacity extending through more than three fourths of the corneal depth).

The present material allows of no conclusions regarding a correlation between a certain site and depth of the opacity on one hand and occurrence of a defect of *Fischer Schweitzer's* pattern on the other.

Five patients (5 per cent of the total series) were even found to have a pathological *Fischer Schweitzer's* pattern but no visible opacity.

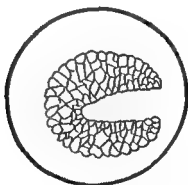


Fig 2

A woman had dendritic keratitis at the age of 43. No recurrence. A follow up 7 years later revealed a large transverse superficial opacity with a ramified offshoot towards 1 o'clock.

Fischer Schweitzer's fluorescein pattern showed peripheral sparing over an area corresponding approximately to that of the opacity whereas the pattern was normal across the offshoot from the opacity.

In two of these cases Fischer Schweitzer's pattern was totally absent (normal pattern contralaterally)

Two showed sparing of the pattern inferiorly at the site of a previous dendritic keratitis as seen in the case record

In one case two islets were seen nasally in the pattern at the site of previous keratitis (fig 3)

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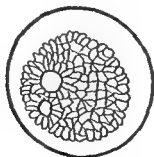


Fig 3

A man had a typical dendritic keratitis nasally of the left eye at the age of 34. At a follow up 11 years later the cornea seemed to be normal (no opacity nor nebulae, not scleral scatter, either no vascularisation nor Hudson-Stahli's line, corneal sensitivity normal)

Fischer-Schweitzer's fluorescein pattern showed two distinct defects at the site of the previous keratitis

The cornea was studied partly in cobalt filtered light (interrupted continuity of the cornea fluoresces because fluorescein penetrates through the rupture) and partly in white light (degenerate cells are stained red by rose bengal)

Vital staining was observed in 35 per cent of the 107 patients who had previously had dendritic keratitis and had now been summoned for a follow up

In two cases a fresh recurrence of dendritic keratitis showing a ramified pattern was found which was stained both by fluorescein and by rose bengal.

In five cases local pathological staining was seen at the site of a previous attack of dendritic keratitis in two cases on account of vesicles in two due to erosion and in one to corneal oedema. All the pathological processes were stained by fluorescein and by rose bengal.

Eight patients presented pronounced extensive punctate fluorescein and rose bengal staining of unknown cause

In three cases fluorescein staining was observed which might be due to the examination itself linear or slightly crescent erosion

19 patients showed punctate rose bengal staining in three cases in a pronounced degree and spread over the whole cornea while in the remaining it was most often localized in a limited space inferiorly and inferonasally as may be seen even in normals

By means of vital staining we disclosed recurrence of dendritic keratitis in two cases pathological processes constituting sequelae of dendritic keratitis in five and abnormal corneae in eleven others out of 107 patients

No correlation was demonstrated between the area of the opacity and the frequency of vital staining

Among the steroid treated vital staining was recorded in 44 per cent against 33 per cent among the IDU treated and the iodine cauterized. This difference may be due to steroid having preferably been prescribed in the grave cases

Permanently dry holes were most frequently found on corneae that were vital stained. This is due to the fact that erosions and vesicles constitute the basis of such holes in the precorneal film. Dry spots were found in 32 per cent of the vital stained corneae whereas in no more than 15 per cent of the total material

Discussion

The present investigation gave the result that the cornea very rarely escapes permanent sequelae of dendritic keratitis

Corneal opacity or nubecula has been found to occur in 85 per cent (Norm 1969 D)

A pathological Fischer-Schweitzer's pattern in the form of a defective or totally absent mosaic has been observed in 79 per cent. In 5 per cent this pa-

thological pattern was not accompanied by opacity. In other words 90 per cent of all the corneae examined displayed opacity and/or a pathological Fischer-Schweitzer's pattern.

The mean wetting time was reduced in these patients likewise indicating that the corneae rarely becomes normal after a dendritic attack.

Permanently dry holes in the precorneal film were found in 15 per cent. In these cases opacity was also seen however. Accordingly this method did not disclose an additional number of pathological cases in the present series. Still further information was obtained on the pathology of the cornea.

In another series I found examples to the effect that residual erosion is only detectable by this method (Norn 1969 B).

At the follow up vital staining revealed active recurrence of dendritic keratitis in 2 per cent. These patients had had a sensation of irritation of the eye for 24 hours and three weeks respectively. No cases were observed of asymptomatic dendritic keratitis.

Pathological vital staining was noticed in several cases (17 per cent) as a sign of a continued pathological state after dendritic keratitis.

These findings showed that even during an apparently recurrence free period with no symptoms the cornea may in many instances be of a poor quality with residual corneal oedema and interrupted continuity of the epithelium a condition which presumably adds to the chance of renewed recurrence.

The present follow up was carried out on a selected series of patients in as far as it only comprised patients referred to a hospital out patient department.

A less severely affected series might possibly contain fewer cases showing pathological changes.

In such a series a follow up examination must however also be expected to reveal several pathological cases when the greatest number available of clinical methods are employed.

To judge from the results of the present study the prognosis of dendritic keratitis is strikingly poor.

The results of corneal sensitivity measurements on the same series will be reported in a final paper.

Summary

A follow up examination of 101 patients who had previously been affected with dendritic (herpetic) keratitis showed the precorneal film to have a reduced wetting time (average 11 seconds against 30 seconds in a normal series measured from concluded blinking to occurrence of a hole in the fluorescein stained precorneal film).

A permanent hole in the precorneal film was found in 15 per cent due to erosion epithelial vesicle keratitis. In some cases it was of unknown cause.

Fischer-Schweitzer's fluorescein pattern was pathological in 19 per cent (totally absent in 7 per cent). In 5 per cent no opacity was seen at the same time. The abnormal pattern was thus the only indication of a pathological process in the cornea concerned and of the site of this.

Vital staining (fluorescein or rose bengal) was observed in 35 per cent. At the time of the follow up 2 per cent had active keratitis, about 15 per cent sequelae of keratitis, in 5 per cent in the forms of vesicle erosion or oedema.

No more than 10 per cent presented no sequelae of the previous dendritic keratitis.

Acknowledgment

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References

- Bron A. J. Correspondence. *Arch Ophthalmol* 79: 119-120 (1968).
Bron A. J. Anterior corneal mosaic. *Brit J Ophthalmol* 52: 609-609 (1968).
Ehlers Niels. The precorneal film (biomicroscopical, histological and chemical investigations). *Acta Ophthalmol suppl* 81: 1-136 (1965).
Fischer F. P. Über die Darstellung der Hornhautoberfläche und ihrer Veränderung im Reflexbild. *Suppl Arch Augenheilk* 98: 1-84 (1923).
Norn M. S. Vital staining in practice using a mixed stain and alcian blue. *Acta Ophthalmol* 42: 1046-1053 (1964).
Norn M. S. Schweitzer's polygonal fluorescein pattern on the cornea (A clinical study and comparison with an applanation - prism - net - phenomenon). *Acta Ophthalmol* 46: 700-711 (1968).
Norn M. S. Desiccation of the precorneal film I. Corneal wetting time. *Acta Ophthalmol* 47: 865-880 (1969 A).
Norn M. S. Desiccation of the precorneal film II. Permanent discontinuity and Dellen. *Acta Ophthalmol* 47: 881-889 (1969 B).
Norn M. S. Dendritic (herpetic) keratitis I (Incidence, season variations, recurrence rate, visual impairment, therapy). *Acta Ophthalmol* 48: 91-107 (1970 C).
Norn M. S. Dendritic (herpetic) keratitis II (Follow up examination of corneal opacity, opacity, vascularisation, Hudson-Stahli's line, sequel of iritis). *Acta Ophthalmol* 48: 213-225 (1970 D).
Schweitzer N. M. J. A fluorescein colored polygonal pattern in the human cornea (the reflectographic Furchenbild of Fischer). *Arch Ophthalmol* 77: 548-553 (1967).
Schweitzer N. M. J. pers. communication.

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LOCALISATION OF BACTERIA ON SINGLE EYELASHES

BY

M S NORN

During an operation one may happen to touch an eyelash with an instrument or suturing material. Further one may not infrequently find an eyelash within the field of operation. How great is the risk of infection during the operation in such cases?

As is well known staphylococci are often present along the palpebral border (Barford, Millansmith *et al*). The contamination of the individual eyelash and the sites of the bacteria on this do not seem to have been examined previously however.

In the course of time attempts have been made in different ways to avoid contamination from the eyelashes during operation.

Pre-operative cutting of the lashes is employed in many places. Allen in a leading article on the practical aspects of ocular infection called attention to the fact that such cutting hardly is of any value in practice. It is perhaps a ritual rather than a rationale.

Newton *et al* advise against cutting because they find that suturing material is more easily caught by the stubble left and because the base of the hair may be infected. Newton recommends sewing of moist gauze bits on to the upper and lower lids to cover all the lashes during the operation.

Elastic covering is perhaps more practical *e.g.* with *steridrapes*.

Some specula are constructed so as to cover the eyelashes as far as possible. Many surgeons apply prophylactic antibiotic ointment the night before the operation

Gowen (1934) showed that bacteria on the eyelid constitute a grave source of infection of the conjunctiva the bacteria being transferred *via* the eyelashes

This route of infection was demonstrated by spreading a culture of *Bacterium prodigiosus* on the skin of the lower lid. The bacteria were recovered on the lashes of the lower lid and in the conjunctiva. Bacteria spread on the upper lid on the other hand were not transferred to the lashes or the conjunctiva. The transfer is supposed to proceed during blinking when the lower row of lashes becomes bent so as to touch the skin

Barfoed (1953) studied the bacterial flora in the conjunctiva and along the palpebral border in 521 cases. Bacteria for culture from the eyelid were obtained by intensive rubbing with a sterile broth moistened cotton swab

Staphylococcus albus were detected on 84.6 per cent of the eyelids and *Staphylococcus aureus* on 23.6 per cent. In the conjunctiva on the other hand the former species were found in no more than 37.5 per cent and the latter in 7.6 per cent. Accordance between the findings on the skin of the eyelid and in the conjunctiva was found in 27 per cent only

The differences between the bacterial flora of the skin and that of the conjunctiva must be supposed to be due to environmental factors. Staphylococci can break down fatty acids being therefore able to live in a sebaceous environment. Staphylococci have their headquarters in pilosebaceous units (Marples)

Inside the eyelid only small amounts of fat are present in the forms of a thin possibly monomolecular fatty layer in the precorneal film (N. Ehlers) and drops of fat on the mucous thread in the inferior conjunctival fornix (Norn 1969 A)

Evidently the mucous layer of the conjunctiva is no optimum environment for staphylococci. Corynebacteria on the other hand do well and in normals these will often oust bacteria coming from the skin

Staphylococci on the palpebral skin may be the cause of blepharitis which nearly always is complicated by conjunctivitis and possibly also of staphylococcus induced punctate or more rarely marginal keratitis (Thygeson 1941 1946). However attempts to combat staphylo blepharitis with mercurial ointment (Penotrase) were unsuccessful in as far as the ointment could not cure the associated staphylococcal infection of the conjunctiva (More 1968)

Hairs are rather often found in the inferior fornix. Thus microscopic examination revealed hairs (eyelashes hairs from eyebrow and elsewhere) in 12 per cent of 198 eyes (Polarisation microscopy - Norn 1969 B)

The object of the present study was to clarify how often the individual eye lash is contaminated and where the bacteria are situated and to map out the resistance pattern of the bacteria

Method

The individual eyelashes were epilated with sterile epilation tweezers singed between each two epilations. The lash was transferred to an agar slide where the root alone was rubbed against the slide over a distance of 3-4 cm. The lash was thereafter laid on the slide in its entire length.

The medium used was Uricult N agar containing beef peptone, liver proteolysate salts and agar (Uricult Orion Helsinki, Finland).

The slide was incubated at 35° for 48 hours.

The slide was examined after 48 hours. The number of bacterial colonies was recorded and the growth of bacteria from the eyelashes and their sites were outlined. The individual colonies were isolated and identified and their resistance was determined.

Material

Examination of four eyelashes from each eye was aimed at one medial and one lateral from the upper lid and one medial and one lateral from the lower.

The investigation comprised 33 eyes from 17 patients. None of these patients showed any signs of infectious conjunctivitis. The clinical diagnoses were retinal detachment in four cases, cataract in four, glaucoma in two, uveitis in one, chronic simple conjunctivitis in one, while five were normal subjects.

Five had not been treated with antibiotics or chemotherapeutics.

Results

In some cases more than one lash was epilated at a time. In 17 cases the two lashes were lying so close together that they presented a common bacterial growth, having therefore been reckoned as one in the report.

In 21 cases an extra isolated eyelash appeared on the slide. This was included in the investigation which accordingly comprised 153 lashes.

Culture revealed *Staph. albus* and a few strains of *Staph. aureus* as well as *Bacterium anthracis*.

The first cultivation on Uricult gave cocci round 119 lashes (77 per cent of the total number).

On further cultivation and resistance determination bacterial growth was seen again in 94 cases (63 per cent).

Staph. albus were isolated from 50 per cent of all the lashes. *Staph. albus*

Some specula are constructed so as to cover the eyelashes as far as possible. Many surgeons apply prophylactic antibiotic ointment the night before the operation.

Gowen (1934) showed that bacteria on the eyelid constitute a grave source of infection of the conjunctiva the bacteria being transferred *via* the eyelashes.

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the root of the lash in agreement with the observation that the hair follicle constitutes the headquarters of *Staph albus*. Note that the tip of the lash more rarely is infected.

The tip of the lash was infected in 18 cases. To these may be added 38 lashes contaminated in their entire length. Thus a total of 56 lashes had bacteria at the tip.

If the lashes had been cut close to the root as is often done pre-operatively there would have been a risk of contamination from the stubble in 52 cases where the root was infected plus 38 cases with the whole lash infected. This gives a total contamination risk from 90 eyelashes.

There is in other words a *theoretically increased risk of contamination after cutting of the lashes*.

For 27 out of 153 eyelashes bacterial colonies were seen in the track on the agar slide after rubbing of the root across the slide. The numbers of colonies were 1-2 in eleven, 3-5 in four, 6-8 in four, 9-10 in four, about 50 in two, 70 in one and about 1000 in one.

Chemoresistance

As shown in table II practically all the *Staph albus* strains were susceptible to erythromycin but often relatively or completely resistant to penicillin and sulphonamide.

44 per cent of the strains were resistant to tetracycline and 43 per cent to chloromycetin while 23 per cent were resistant to streptomycin.

The patients not treated previously with antibiotics or chemotherapeutics showed approximately the same resistance pattern (table II).

The few *Staph aureus* strains found were susceptible to all the antibiotics tried except two strains which were resistant to penicillin.

We may conclude that rational treatment against bacteria on the eyelashes can be carried out with erythromycin while chloromycetin and tetracycline are less suitable and penicillin and sulphonamide unsuitable.

Discussion

The finding of many chloromycetin resistant *Staph albus* strains was surprising.

In 1963 Cregersen studied the resistance pattern of bacteria isolated from

were found on one or more lashes from all the patients except one who in turn harboured *Staph aureus*

In four eyes *Staph albus* were not detected while 15 eyes showed one *Staph albus* strain and seven two different strains to judge from the chemoresistance pattern. Four eyes harboured three strains. Finally, four five and six strains with different patterns were detected in one eye each.

In 14 eyes there were found not less than two *Staph albus* strains with different chemoresistance patterns judged by examination of four eyelashes or more from each eye. On an average 2.9 strains were found per eye. The numbers of strains averaged 1.7 on the upper lid and 1.9 on the lower. Further the medial pair of lashes contained on an average 1.9 strains and the lateral 1.7 strains.

The figures suggest that the various eyelashes of an individual may harbour two or more staphylococcal strains accumulated within different parts of the row of lashes.

Staphylococcus aureus were found in 5 per cent of all the lashes namely in four eyes of three patients. Two patients harboured only one phage type each (type 52/80 u and 42 E/47/53/54/75/77/83 A/84/85/6077/92).

In the third patient there were found two phage types in one eye (52/52 A/80 and 84/6551/592) and a different phage type in the other eye (3 Cu).

Thus five phage types were seen.

In one eye there were found two *Staph aureus* strains differing in susceptibility while in the remaining eyes only one pattern was seen.

Bact antratum were isolated from 1 per cent of all the eyelashes i.e. in two eyes of two patients with only one resistance pattern per eye.

The site of the bacterium on the epilated eyelash is shown in table I. It is seen in the table that the bacteria most often are localized in or round

Table I
Sites of the bacteria on the epilated eyelash

	<i>Staph albus</i>	<i>Staph aureus</i>	Total
primary growth from the root	47	5	52
middle of the shaft	10	1	11
the tip	18	0	18
the whole length	36	2	38
Total	111	8	119

the root of the lash in agreement with the observation that the hair follicle constitutes the headquarters of *Staph albus*. Note that the tip of the lash more rarely is infected.

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In 1943 Cregersen studied the resistance pattern of bacteria isolated from

Table II
Resistance pattern of bacterial strains cultured from eyelashes

	number of strains	penicil	sulpha	strepto	tetra	chloromyc	erythr
<i>Staph aureus</i>	9	2	0	0	0	0	0
<i>Staph albus</i>	128	105	98	30	56	55	2
<i>Staph albus</i> in per cent	128	82	77	23	44	43	2
<i>Staph albus</i> from non anti- biotic treated pls in per cent	42	81	83	19	40	38	0

the nasal mucosa of employees doctors and nurses attached to the Department of Ophthalmology Kommunehospitalet. He found 26 *Staph aureus* strains all susceptible to chloromycetin and 26 *Staph albus* strains of which only three were resistant to chloromycetin.

S. E. Lorentzen in a similar investigation from 1967 achieved practically the same results as Gregersen (only one chloromycetin resistant *Staph aureus* strain out of 14).

Lorentzen concluded that though chloromycetin has been used as the antibiotic of choice in this Department since 1957 chloromycetin resistant *Staph aureus* strains have not developed in the nasal flora of the staff living in a chloromycetin containing environment.

The observation of 43 per cent resistant *Staph albus* strains cultured from eyelashes raises suspicion of development in the unit of chloromycetin resistant strains. This development is possibly related to increasing use of chloromycetin also as a drug for general oral treatment. It will therefore be a matter of interest to undertake another examination in a few years of the nasal flora in this unit.

The investigation showed that *Staph albus* is a very frequent finding on the individual eyelash. It is therefore surprising that surgical intervention is so rarely followed by intra ocular infection.

The explanations of this must be that *Staph albus* usually is apathogenic and that the protective apparatus of the conjunctiva is rather efficient. The most important protective agents are lysozyme in the tears, antibody, leucocyte phagocytosis and competing bacteria.

One may also wonder that staphylococci are not always present in the conjunctiva. This may be due not only to the above factors but also to removal by transportation with the tears and with mucus via the mucous thread in the lower conjunctival fornix (Norn 1969 A).

The results of the present investigation suggest that the majority of staphylococci are situated in and round the hair root whereas relatively fewer bacteria are found at the tip of the hair.

The operative cutting of the eyelashes therefore cannot be taken to reduce the number of bacteria.

However, if the lashes lie bare within the field of operation it may often be necessary to cut them for purposes of space.

Summary

A total of 153 single eyelashes epilated from 33 eyes of 14 patients have been subjected to bacteriological examination.

Table 11
Resistance pattern of bacterial strains cultured from cyclashes

	number of strains	penicil	sulpha	strepto	tetra	chloromyc	erythr
<i>Staph aureus</i>	9	2	0	0	0	0	0
<i>Staph albus</i>	125	105	98	30	56	55	2
<i>Staph albus</i> in per cent	128	62	77	23	44	43	2
<i>Staph albus</i> from non anti- biotic treated pts in per cent	42	81	83	19	40	36	0

We considered if our patient might suffer from optic neuritis as a manifestation of a demyelinating lesion. Her normal vision and normal visual fields were to some extent against this assumption.

Daroff & Laaton Smith (1965) reported on three patients with optic neuritis and normal visual acuity but field defects were present and the cases were unilateral as distinct from ours.

Chamlin (1953) collected 100 cases of optic neuritis. Among these the visual acuity was normal in 21% and only slightly impaired in another 16%. All these patients revealed field defects although they were only small and of peripheral distribution in some cases. Unfortunately the author did not state the frequency of papilloedema but it must have been present in some of the patients since he concluded: 'This is corroborative evidence that the preservation of central visual acuity alone must not be used as a major criterion for differentiating optic neuritis from other conditions such as papilloedema.' It appears from the paper that there were several bilateral cases of optic neuritis but the number is not stated.

François (1956) discussed the differential diagnosis of *papillitis* and *choked disc*. He reported six cases of papilloedema. The visual acuity was normal but all the patients had field defects. In one case the papilloedema was bilateral and the field defect in one eye was doubtful but as the patient had concurrent hypertension the findings are difficult to assess.

Roper Hall (1958) reported five cases of optic disc oedema associated with normal visual fields and near normal visual acuity and absence of increased intracranial pressure. He interpreted this combination as a *nutritive phenomenon* on the assumption that when the ratio of the arterial to the venous pressure in the retina is 3:2 instead of 3:1 this will result in malnutrition and hence oedema of the disc. He expressed the view that this is the case in partial venous thrombosis, malignant hypertension, Guillain Barre's syndrome and hypotension occurring after head injury. Even though it is not quite unlikely this explanation must be taken with some reserve as the assumption is of a purely hypothetical nature as long as the available measuring methods are relatively inaccurate.

According to studies by François (1956) and Chamlin (1959) vitreous opacities suggest optic neuritis (*papillitis*) but not choked discs.

As our patient had normal blood pressure hypertensive changes can be ruled out.

Bilateral central vein thrombosis referable to hypertension and arteriosclerosis is not uncommon but in our case there was no evidence in favour of this diagnosis.

Another diagnostic possibility was retinal vasculitis. *Retinal vasculitis* or *reticulitis* is not a well defined disease entity. It comprises retinal vascular lesions of widely different aetiology and morphology. Thus Baillentine &

Lumbar puncture revealed a pressure of 650 mm H₂O (sitting position) and 84 mg% protein leukocytes 114 spinal sugar normal

The neurological signs were aggravated during the next 6 weeks and several lumbar punctures showed unchanged conditions. The patient was treated with corticotrophin which resulted in an improvement in the gait but the patient still had to walk with two sticks.

Ophthalmological examination showed a visual acuity of 6/7.5 + 1.0 in the right eye and 6/10 + 1.0 in the left. The position and direction of the eyes were normal and the ocular movements were unimpeded in all directions. No nystagmus or jerky ocular movements. The corneal sensibility was normal. The pupils were of equal size in maximal mydriasis.

Slit lamp examination showed that the corneae were clear. A fine aqueous flare was seen in the anterior chamber on both sides and numerous opacities of the vitreous were present. Ophthalmoscopy revealed oedema and pronounced hyperaemia of both discs with a swelling of 1 dioptr. The veins were very dark, greatly dilated and tortuous with periphlebitis centrally and peripherally. Colour sense normal. Field of vision 5/1000 red/white normal.

An examination performed 5 days later showed haemorrhages at the margins of the discs and the ophthalmoscopic appearance was still characterised by considerable venous stasis. Field of vision normal. During the next few months the venous stasis decreased and the haemorrhages, vitreous opacities and the aqueous flare gradually subsided.

The patient returned for a check up examination 11 months after the onset of the disease. The gait was now practically normal and the neurological manifestations had disappeared. The visual acuity was 6/6 + 0.5 in both eyes. Ophthalmoscopy showed well defined discs with a few newly formed vessels at the margins. There was no vascular stasis but some residual periphlebitis was present. Visual fields normal.

Discussion

At the first examination of our patient the ophthalmoscopic findings were strongly suggestive of choked discs but the presence of a normal pressure on lumbar puncture weighed against a diagnosis of choked discs caused by a space occupying intracranial lesion. The diffuse neurological symptoms with bilateral sensory and motor deficits were in favour of a disseminated disease.

In his survey of the literature on *choked discs and spinal tumours* Newman (1958) reported some cases in which tumours of the cervical spine produced choked discs because of retrograde brain oedema. In the present case the clinical picture and the normal cervical cord revealed by pneumoencephalography militated against the presence of such a tumour.

Stapford (1951) reported a number of cases of supratentorial tumours associated with *choked discs and normal intracranial pressure* but his explanation viz. obstructed venous drainage is not acceptable. However there was no evidence in favour of such a tumour in our patient.

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Michaelson (1937), Duke-Elder (1967) and others included Eales disease in which vitreous haemorrhages occur under this heading. On the other hand Sorsby (1963) differentiated retinal vasculitis from Eales disease just because of the vitreous haemorrhages in the latter. Lyle & Wjbar (1961) occupy an intermediate position: they divided vasculitis into two groups: one with peripheral retinal changes and another characterised by changes in the central vein especially complete or partial thrombosis. Lyle & Wjbar (1961) reported a case in which there were peripheral changes in one eye and central changes in the other. This should be suggestive of an *auto-immune process*.

Miescher *et al* (1968) studied the immunological changes in the skin in vasculitis by immune fluorescence technique. He concluded "Each phenomenon may serve as a control for the findings in other immune phenomena".

Eales disease with large vitreous haemorrhages is very similar to a Schwartzmann phenomenon. It is usually bilateral with a fairly great time lag for the occurrence in the second eye. This points in the direction of an auto-immune disease. Lyle & Wjbar (1961) published a total of seven cases of retinal vasculitis including two which were bilateral. One of these was that mentioned above, the second showed changes mainly suggestive of thrombosis of the central retinal vein. Only in the presence of macular haemorrhages did severe visual impairment occur. None of these patients had neurological manifestations.

Lonn & Hoyt (1966) published five cases of unilateral papilloedema with distinct signs of involvement of the central retinal vein: the patients were otherwise healthy young men. The authors expressed the view that the designation "retinal vasculitis" is unnecessarily general and may comprise a number of different diseases and they suggested that a special group should be segregated viz. cases characterised by papilloedema, normal or near normal visual acuity, normal visual field, dilated veins and scattered peripheral haemorrhages and that this entity should be called *papillophlebitis*, a term which seems adequate.

Another problem faced in our case was the relationship between the uveitis and the neurological manifestations.

First it must be emphasised that the eye is developed from all three germ layers. Accordingly allergic disorders in all groups of tissue can result in similar processes in the eye as is seen for example in rheumatic diseases, allergic skin disorders and many other groups of diseases. Secondly it should be mentioned that the uvea and retina apparently contain identical antigens and it is therefore impossible to differentiate these two organs in allergic affections. Owing to the intimate anatomical relationship between the uvea and retina an affection of one of the two organs will also often involve the other.

Both from a clinical and an immunological point of view there is thus an intimate relation between uveitis and demyelinating processes in the central nervous system.

Braak & Herwaarden (1933) published a survey in which they reported six cases of ophthalmencephalomyelitis of their own and discussed the causes of the unquestionable relationship between demyelinating lesions in the central nervous system and pathological findings in the eye especially those localised in the vessels of the uvea and retina. They expressed the view that the cause of this relationship is a combination of an infection and immunological processes.

As distinct from those in the central nervous system the lesions of the eye are not of a permanent nature because the eye does not contain myelin sheaths the process is therefore arrested at the ocular vessels and does not result in permanent loss of function.

In our patient periphlebitis was seen in several places along the retinal veins. It is now generally recognised that this is a common finding in patients with multiple sclerosis. It was first described by Haarr in 1951 and later by Rucker (1954) who observed it in 10% of his patients. Møller & Hammerberg (1963) reported that retinal periphlebitis is present in up to 20% of patients with multiple sclerosis.

In their paper of 1933 Braak & Herwaarden described ophthalmoscopic observations which must have been manifestations of retinal periphlebitis. In 1965 Fog published histological studies of the eye and central nervous system in patients with multiple sclerosis. He found that the retinal periphlebitis and the pathological vascular changes in the central nervous system are of the same nature and concluded: 'From the point of view of pathological anatomy multiple sclerosis is a condition of periphlebitis cerebrospinalis and retinalis. As encephalomyelitis is also a demyelinating lesion it is reasonable to assume that his conclusion also applies to this disease.'

Iridocyclitis is a condition which is not uncommon in patients with multiple sclerosis. Thus Tschabitscher *et al* (1967) found this complication in 5.5% of their patients. Haarr (1961) reported that 4.5% of his patients with iridocyclitis suffered from multiple sclerosis and Bech (1961) found multiple sclerosis in 4% of his cases of chronic iridocyclitis. These percentages are so high as compared with normal series that they must represent a significant difference.

There are many points of resemblance between uveoretinal affections and demyelinating lesions in the central nervous system. In the aetiology of these disorders we must consider both infectious factors particularly virus infections and the possibility of antigen-antibody formation. In addition auto-immune factors must be taken into account and finally a patho-anatomical comparison must be made.

Pette & Pette (1963), Ross *et al* (1965) and Wright *et al* (1965) performed immunological studies on patients with multiple sclerosis and other demyelinating lesions. There seems to be a certain agreement between the results of these

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Both from a clinical and an immunological point of view, there is thus an intimate relation between uveitis and demyelinating processes in the central nervous system.

Summary and Conclusions

The purpose of the study here was through a comparison of the available literature and the findings in the case reported above to find out if there is a common pathogenic basis for demyelinating lesions in the central nervous system and diseases of the uvea. The reasons outlined below are in favour of the existence of such a relationship.

1 The frequency of simultaneous occurrence of these diseases is so high that it must be significant and cannot be due to mere chance.

2 Concurrent development of these diseases can be induced experimentally by the injection of a single causative agent.

3 Good agreement exists between the experimental results obtained by neurologists and ophthalmologists in the study of antigen antibody formation and auto immunisation as factors in the pathogenesis of these disorders.

4 As is well known both uveitis and demyelinating lesions occur simultaneously as complications of a number of common virus diseases such as measles and herpes zoster.

5 Signs of thrombotic processes in the central vein of the retina in both eyes were observed in our patient with a demyelinating lesion. This also shows the interdependence assumed in the theory that thrombosis of the small veins of the central nervous system may be the cause of demyelinating lesions.

The reason why the term demyelinating lesion is used throughout this paper instead of a definite diagnosis within this group of diseases is that it could not be unquestionably determined if our patient suffered from disseminated encephalomyelitis or multiple sclerosis only the further course of the disease and particularly future seizures if any will reveal the exact diagnosis.

The considerations set forth here must not be taken as proof of the theory of a common pathogenesis of the diseases in question but the case reported lends support to this theory since it revealed definite thrombotic processes in the venous system of the retina in a patient with a demyelinating disease.

References

- Agar, I. L. P. et al. Pathogenesis of iridocyclitis. *Orient Arch Ophthalmol* 1 (1963) 19.
Ballantyne, I. J. & MacLachlan, I. C. A case of perivascularitis retinae associated with symptoms of central disease. *Brit J Ophthalmol* 1 (1937) 7.
Berch, A. Chronic iridocyclitis. *Acta Ophthalmol* 29 (1951) 363.
Bendstrup, I. Central retinal vein thrombosis and haemorrhagic glaucoma. Munksgaard, Copenhagen, 1950.
Björk, W. Immunpathologie des Auges. *Bibl Ophthalmol* No. 4. S. Karger, Basel, 1963.
Bruck, J. V. K. & van Herwaarden, J. Ophthalmocerebralomyelitis. *Klin Monatsheft Augheilk* 91 (1954) 316.

authors and those obtained by *Agarwal et al* (1963) in their studies of the aqueous humour in patients with uveitis

Boke (1968) advanced a theory of the auto immune process occurring in the uvea infection of the uvea leading in turn to uveitis production of uveotropic antibodies and finally, to auto immune uveitis This sequence represents a vicious circle and ultimately results in uveitis of the other eye This theory also explains the time lag not infrequently seen in the involvement of the second eye in bilateral chronic uveitis Thus *Beck* (1961) found that there was a time interval of more than 12 months between the development of the disease in the two eyes in 20 % of 106 patients with chronic bilateral uveitis In experiments on pigs *Fog & Bardram* (1953) induced concurrent encephalitis and uveitis by injection of homologous and heterologous brain extract

In the discussion of the relation between multiple sclerosis and uveitis it must be emphasised that the frequent finding of vitreous opacities in optic neuritis (papillitis) is an important sign in the differential diagnosis of this disease from choked discs since such opacities suggest involvement of that portion of the uvea which is adjacent to the optic nerve

As already mentioned *Fog* (1965) published a histological study on retinal periphlebitis in which he found a great similarity between the changes observed and those occurring along the veins in multiple sclerosis It must however be added that none of these changes are specific In multiple sclerosis thrombosis occurs in some of the veins in the affected portions of the cerebrum and spinal cord In older cases of uveitis histological examination will also disclose thrombosis of some of the veins In our case the ophthalmoscopic appearance was suggestive of venous thrombosis as evidenced by the choked discs considerable venous stasis and haemorrhages although these were not so extensive as is usually seen in central vein thrombosis Cases with a similar ophthalmoscopic appearance were described by *Lyle & Wybar* (1961) and *Lonn & Hoyt* (1966)

The neovascularisation observed in the vicinity of the discs is suggestive of the development of collaterals It must thus be presumed that the retinal circulation was re established partly through the collaterals and partly by a recanalisation of the central vein That our patient regained normal vision after a transient impairment is in agreement with the observations of *Lyle & Wybar* (1961) and *Lonn & Hoyt* (1966)

In his study of central vein thrombosis *Brændstrup* (1950) found that it is principally in relatively young individuals that normal or near normal vision returns after the acute phase of the disease has passed off In our patient an acute catastrophe which is seen in so many cases of central vein thrombosis did not occur, and the relatively small number of haemorrhages suggests that the central vein thrombosis was only partial or that it developed so slowly that the compensatory factors operative in the re establishment of circulation went into action so early that the destructive processes in the retina were eliminated

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References

- Agarwal L. I. et al. Pathogenesis of iridocyclitis. *Orient. Arch. Ophthalmol.* 1 (1963) 19.
 Ballantyne A. J. & Michaelson I. C. A case of perivascularitis retinae associated with symptoms of central disease. *Brit. J. Ophthalmol.* 1 (1937) 72.
 Bril A. Chronic iridocyclitis. *Acta Ophthalmol.* 39 (1961) 363.
 Brandrup P. Central retinal vein thrombosis and haemorrhagic glaucoma. Munksgaard Copenhagen 1959.
 Burke W. Immunopathologie des Auges. *Bibl. Ophthalmol.* No. 8 S. Karger Basel 1963.
 de Baat C. F. K. & van Herwaarden J. Ophthalmoencephalomyelitis. *Ned. Maandbl. Augenheilk.* 31 (1933) 316.

- Chamlin M Visual field changes in optic neuritis Arch Ophthal 50 (1953) 699
- Chamlin M Aqueous floaters in the differential diagnosis of papillitis and papilledema Arch Ophthal 61 (1959) 37
- Daroff R B & Lauson Smith J Intraocular optic neuritis with normal visual acuity Neurology 15 (1965) 409
- Duke Elder S System of Ophthalmology vols I & II 1967
- Fog T The topography of plaques in multiple sclerosis Acta neurol Scandinav 41 Suppl 15 1965
- Fog T & Bardram M Experimentel encephalomyelitis og iridocyclitis hos grise Nord Med 49 (1953) 851
- François J et al Diagnostic differential entre la papillite a vision normale et la stase papillaire Ann d'ocul 189 (1956) 669
- Haarr M Uveitis with neurological symptoms Acta Ophthal 39 (1961) 60
- Haarr M Periphlebitis retinae ved sclerosis multiplex Akademisk Trykningsentral Oslo 1951
- Lonn L I & Høyt W F Papillophlebitis Eye Ear Nose & Throat Monthly 40 (1966) 62
- Lyle T A & Wybar K Retinal vasculitis Brit J Ophthal 45 (1961) 718
- Miescher A et al Vascular disease in ophthalmology Bibl Ophthal No 16 S Karger Basel 1968
- Møller P M & Hammerberg P E Retinal periphlebitis in multiple sclerosis Acta neurol Scandinav 39 Suppl 4 (1963) 263
- Newman E W Ocular signs of intracranial disease in children and juveniles A report of 42 cases Am J Ophth 21 (1958) 286
- Pette E & Pette H Some remarks on the pathogenesis of demyelinating disease J Neuropath & Exper Neurol 22 (1963) 528
- Roper Hall M J Optic disc oedema in the absence of raised intracranial pressure Brit J Ophth 42 (1958) 91
- Ross C et al Infective agents and multiple sclerosis Brit M J I (1965) 226
- Rucker C V Posterior uveitis as a manifestation of multiple sclerosis Mayo Clin Proc 40 (1964) 544
- Sorsby A Modern Ophthalmology vol IV 1964
- Stapford J S B Increased intracranial pressure Brain 51 (1928) 465
- Tschabitscher et al Wien med Wchnschr 112 (1962) 279
- Wacker B W et al Vascular diseases in ophthalmology Bibl Ophthal No 16 S Karger Basel 1968
- Wacker B W et al The immunologic responses of rabbits to homologous and heterologous corneal and uveal tissues J Immunol 96 (1961) 690
- Walsh F B Clinical Neuroophthalmology Williams & Wilkins Baltimore 1957
- Wright R et al Immunological studies in multiple sclerosis Incidence of circulating antibodies of dietary proteins and auto antigens Brit M J I (1965) 491
- Wybar K C The ocular manifestations of disseminated sclerosis Proc Royal Soc Med 45 (1952) 315

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SKLERALINDENTATION UND PHOTOKOAGULATION

VON

F FANKHAUSER und W LOTMAR

1 Einleitung

Bei der Photokoagulation pra aquatoraler Netzhautveränderungen ist eine gelaufene Erfahrung, dass die Behandlung durch Skleral Indentation (SI) wesentlich erleichtert oder überhaupt erst möglich wird. Die Vorteile der SI, die von Cibis (1) und Crignolo (2) ausführlich gewürdigt wurden, sind kurz die folgenden:

- a) Netzhautareale, die normalerweise der Beobachtung nicht zugänglich sind, werden in das Gesichtsfeld verschoben und können behandelt werden.
- b) Die Pulsenergie, die zur Erzielung einer klinisch ausreichenden Photokoagulation notwendig ist, kann über einem eingedellten Netzhautbezirk reduziert und damit die Strahlenbelastung der Augenmedien herabgesetzt werden.
- c) Die Bildqualität im Beobachtungssystem wird verbessert und damit die Schnelligkeit und Sicherheit der Photokoagulation merklich erhöht.

Bei der konventionellen Photokoagulation ohne Kontaktglas wird die SI auf einfache Weise durch stabchenförmige Eindellungssporne erreicht. Koaguliert man durch das Kontaktglas (Fankhauser & Lotmar (3)), so muss an diesem eine Eindellungsvorrichtung angebracht sein. Es stehen die Eindellungskontaktgläser von Clummann & Schmidt (4), der mit dem Goldmann Kontaktglas zusammen

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- Chamlin M* Visual field changes in optic neuritis *Arch Ophthalmol* 50 (1953) 699
- Chamlin M* Aqueous floaters in the differential diagnosis of papillitis and papille dema *Arch Ophthalmol* 61 (1959) 37
- Daroff R B & Lawton Smith J* Intraocular optic neuritis with normal visual acuity *Neurology* 15 (1965) 409
- Duke-Elder S* System of Ophthalmology vols I & II 1967
- Fog T* The topography of plaques in multiple sclerosis *Acta neurol Scandinav* 41 Suppl 15 1965
- Fog T & Bardram M* Experimentel encephalomyelitis og iridocyclitis hos grise *Nord. Med* 49 (1953) 851
- François J et al* Diagnostic differential entre la papillite = vision normale et la stase papillaire *Ann d'ocul* 189 (1956) 669
- Haarr M* Uveitis with neurological symptoms *Acta Ophthalm* 39 (1961) 60
- Haarr M* Periphlebitis retinae ved sclerosus multiplex *Akademisk Trykningsentral Oslo* 1951
- Lonn L I & Hoyt W F* Papillophlebitis *Eye Ear Nose & Throat Monthly* 45 (1966) 62
- Lyle T K & Wybar K* Retinal vasculitis *Brit J Ophthalm* 45 (1961) 718
- Miescher A et al* Vascular disease in ophthalmology *Bibl Ophthalm* No 16 S Karger Basel 1968
- Moller P M & Hammerberg P E* Retinal periphlebitis in multiple sclerosis *Acta neurol Scandinav* 39 Suppl 4 (1963) 263
- Neuman E W* Ocular signs of intracranial disease in children and juveniles A report of 42 cases *Am J Ophthalm* 21 (1959) 256
- Pette E & Pette H* Some remarks on the pathogenesis of demyelinating disease *J Neuropath & Exper Neurol* 22 (1963) 528
- Roper Hall M J* Optic disc oedema in the absence of raised intracranial pressure *Brit J Ophthalm* 42 (1958) 91
- Ross C et al* Infective agents and multiple sclerosis *Brit M J* 1 (1965) 226
- Rucker C V* Posterior uveitis as a manifestation of multiple sclerosis *Mayo Clin Proc* 40 (1964) 544
- Sorsby A* Modern Ophthalmology vol IV 1964
- Stapford J S B* Increased intracranial pressure *Brain* 51 (1928) 485
- Tschabitscher et al* *Wien med Wchnschr* 112 (1962) 219
- Wacker B W et al* Vascular diseases in ophthalmology *Bibl Ophthalm* No 16 S Karger Basel 1968
- Wacker B W et al* The immunologic responses of rabbits to homologous and heterologous corneal and uveal tissues *J Immunol* 86 (1961) 690
- Walsh F B* Clinical Neuroophthalmology *Williams & Wilkins Baltimore* 1957
- Wright R et al* Immunological studies in multiple sclerosis Incidence of circulating antibodies of dietary proteins and auto antigens *Brit M J* 1 (1965) 491
- Wybar K C* The ocular manifestations of disseminated sclerosis *Proc Royal Soc Med* 45 (1952) 315

II Aufgabe

Im folgenden ist der Versuch unternommen worden auf Grund von Strahlendurchrechnungen durch ein theoretisches Augenmodell bis zu hohen Werten des Gesichtswinkels angenähert quantitative Aussagen über die Wirkung der SI auf die optischen Verhältnisse bei der Photokoagulation zu gewinnen. Die Ergebnisse gelten dabei dem Sinne nach in gleicher Weise für die konventionelle Methode wie für die Koagulation durch das Kontaktglas von Goldmann.

Das zugrundegelegte Augenmodell wird an anderer Stelle eingehend beschrieben (Lotmar (9)). Die hier interessierenden Zusammenhänge sind im wesentlichen die Abhängigkeit der scheinbaren Pupillengrösse und des Auftreffwinkels auf der Netzhaut vom Gesichtswinkel des einfallenden Strahlenbündels. Abb. 2 erläutert die verwendeten Winkelbezeichnungen. Als Gesichtswinkel wird hier der Winkel zwischen der optischen Achse und dem einfallenden durch die Pupillenmitte gehenden Hauptstrahl definiert. Die Strahlendurchrechnung liefert die zugehörigen Winkel der Hauptstrahlen nach Passieren der Linse, sodass bei bekannter Form des Augapfels die Auftreffwinkel auf der Netzhaut graphisch bestimmt werden können. Für die Form des Auges wurden die Angaben von Le Grand (10) übernommen. Aus der Durchrechnung weiterer Strahlen kann auch der Wert des bei schiefem Durchtritt verkürzt erscheinenden Pupillendurchmessers erhalten werden. Die Ergebnisse stimmen mit den von Jay (11) experimentell erhaltenen gut überein.

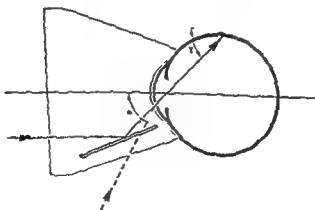


Abb. 2

Strahlengang und Brechungen im System Auge plus Kontaktglas (mit Spiegel) a
Gesichtswinkel Auftreffwinkel Gestrichelt: Fallrichtung des Hauptstrahls ohne
Kontaktglas

wirkende Eindellungstrichter von Eisner (5, 6) und dessen Variation nach Linder (7) sowie das Eindellungkontaktglas von Fankhauser & Lotmar (8) zur Verfügung

Das mit dem Eindellungstrichter von Eisner versehene Goldmannglas hat sich in unseren Händen in der klinischen Praxis am besten bewährt. Mit der Version von Linder haben wir keine Erfahrung. Das Kontaktglas von Fankhauser & Lotmar ist schematisch in Abb. 1 dargestellt. Es weist als einziges einen kontinuierlich verstellbaren Dorn auf, bedarf aber noch weiterer Verbesserungen, bis es klinisch auf breiter Front verwendet werden kann.

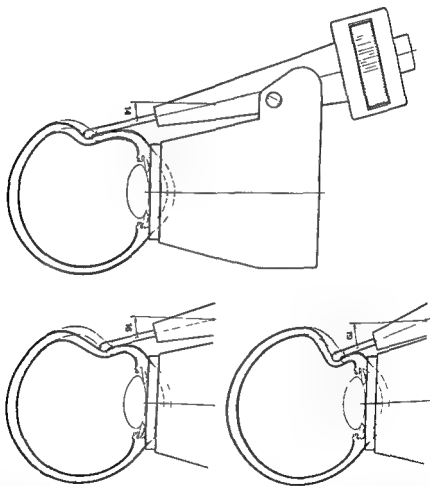


Abb. 1

Schematische Darstellung der Eindellung durch den beweglichen Dorn des Kontaktglases nach Fankhauser & Lotmar für drei verschiedene Neigungswinkel und je zwei Ausfahr-Stellungen. Stärke der Eindellung ca 3,5 bzw. 2,5 mm.

* Zu beziehen bei Firma E. Huber Stockli, Mechan. Werkstätte Seftigenstr. 71, CH 3123 Belp.

II Aufgabe

Im folgenden ist der Versuch unternommen worden auf Grund von Strahlendurchrechnungen durch ein theoretisches Augenmodell bis zu hohen Werten des Gesichtswinkels angenähert quantitative Aussagen über die Wirkung der SF auf die optischen Verhältnisse bei der Photokoagulation zu gewinnen. Die Ergebnisse gelten dabei dem Sinne nach in gleicher Weise für die konventionelle Methode wie für die Koagulation durch das Kontaktglas von Goldmann.

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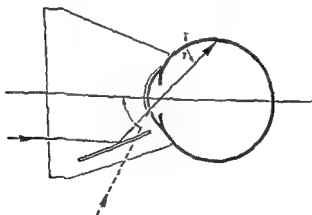


Abb. 2

Strahlengang und Berechnungen im System Auge plus Kontaktglas (mit Spiegel) a Gesichtswinkel i Auftreffwinkel r Winkel des Hauptstrahls ohne Kontaktglas

Die Form des Augapfels bei Eindellung (Abb 1) wurde nach Plausibilitäts Überlegungen dargestellt. Die Bestimmung des Auftreffwinkels sowie die Annahme darüber welcher Punkt der nicht eingedellten Bulbuswand sich auf der Kuppe des Lendeldorns befindet ist daher mit einiger Unsicherheit behaftet. Die im folgenden gegebenen diesbezüglichen Kurven sind nur als halb quantitativ zu betrachten und sollen eine erste Annäherung darstellen.

III Die verschiedenen Wirkungen der Eindellung

1 Scheinbarer Pupillendurchmesser

Die Kurve der Abb 3 gibt an um wieviel sich der Gesichtswinkel α ändert, wenn eine Stelle der Netzhaut um 2,5 mm eingedellt wird. Diese Änderung beträgt beispielsweise für diejenige Stelle welche ohne Eindellung einem Gesichtswinkel von 90° entspricht ca 19° d. h. dieselbe Stelle wird nach Eindellung von dem unter 71° einfallenden Bündel getroffen. In Abb 4 ist dargestellt, wie sich diese Änderung bezüglich der für die Koagulation nutzbaren kleinen Pupillenachse auswirkt. Während Kurve (a) die Pupillenbreite für das normale Auge als Funktion des Gesichtswinkels angibt wobei ein Durchmesser von 8 mm angenommen wurde zeigt Kurve (b) die Breite für die entsprechenden eingedellten Netzhautstellen. Man sieht dass beispielsweise bei 90° Gesichtswinkel die Breite ohne Eindellung 1,5 mm beträgt bei Eindellung der betreffenden Stelle jedoch 3,7 mm was wie es sein muss dem Wert für den Einfallswinkel 71° der Kurve (a) entspricht. Da die Energie eines auf die Netzhaut fokussierten

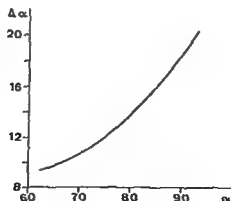


Abb 3

Effektive Verminderung des Gesichtswinkels auf einer um 2,5 mm eingedellten Netzhautstelle die ohne Eindellung von dem unter dem Winkel α (Abszisse) einfallenden Hauptstrahl getroffen wird

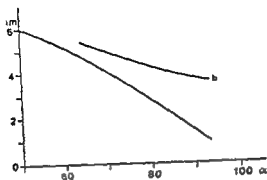


Abb. 1

Kleine Achse der elliptischen Pupille in Funktion des Gesichtswinkels Kurve a Für nicht eingedelltes Auge und Pupillendurchmesser von 8 mm (nach Jay) Kurve b Für die entsprechenden Netzhautstellen bei Lindellung um 2.5 mm

Koagulationsbündels von kreisförmigem Querschnitt quadratisch mit seinem Durchmesser in der Pupille zunimmt so entsprechen die in diesem Beispiel angegebenen Zahlen einem Energiegewinn um das Sechsfache

2. Verringerung des Abstands der Netzhaut von der Pupille

Wie aus Abb. 1 unmittelbar anschaulich hervorgeht kommt eine eingedellte Netzhautstelle auf dem sie treffenden Hauptstrahl wesentlich näher zur Pupille zu liegen als diejenige Stelle welche vom selben Hauptstrahl ohne Lindellung erreicht wird. Ein auf die eingedellte Stelle fokussiertes durch die Pupille im Querschnitt begrenztes Koagulationslichtbündel weist also einen grossen Kegeiwinkel d. h. eine höhere numerische Apertur auf als ohne Lindellung. Da die damit verbundene Energiesteigerung im Fokus ebenfalls quadratisch mit der Abstandsverminderung wächst ist auch dieser Effekt sehr wirksam. Dabei ist zu beachten dass bei der bisher üblichen Art der Koagulation mit parallel ins Auge fallendem Strahlenbündel sammelnde Vorsatzlinsen verwendet werden sollten da ja sonst eine Defokussierung auftritt welche den erwarteten Energiegewinn zu nichte macht. Bei der Koagulation durch das Kontaktglas sind dagegen keine Zusatzlinsen erforderlich indem durch Führung der Optik nachfokussiert werden kann. Im übrigen kann natürlich die Möglichkeit einen Lichtkegel grosserer Apertur durch die Pupille zu bringen bei bereits genügender Energie auch dahin ausgenutzt werden dass man die Apertur nicht vergrössert dafür aber eine gewisse Bewegungsfreiheit in der Pupille gewinnt was bei der stets mehr oder weniger vorhandenen Instabilität des Systems Arzt Apparat Patient sehr wünschenswert ist.

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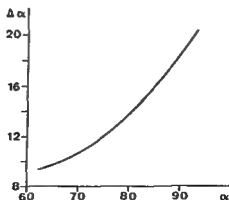


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Effektive Verminderung des Gesichtswinkels auf einer um 2.5 mm eingedellten Netzhautstelle die ohne Eindellung von dem unter dem Winkel α (Abszisse) einfallenden Hauptstrahl getroffen wird

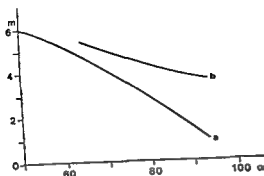


Abb 4

kleine Achse der elliptischen Pupille in Funktion des Gesichtswinkels kurve a für nicht eingedelltes Auge und Pupillendurchmesser von 8 mm (nach Jay) kurve b für die entsprechenden Netzhautstellen bei Eindellung um 2,5 mm

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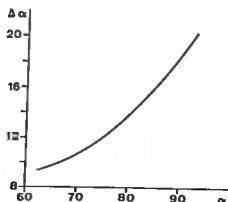


Abb 3

Effektive Verminderung des Gesichtswinkels auf einer um 2,5 mm eingedellten Netzhautstelle die ohne Eindellung von dem unter dem Winkel α (Abszisse) einfallenden Hauptstrahl getroffen wird

ung der Zirkulation durch Eindeilen keine Rolle Beim Arbeiten mit koninuerlichem Xenonbogen wo die Pulsdauer in der Grossenordnung von 1 sec liegt wird dagegen dieser Einfluss merkbar sein d h die Eindeilung wird den Wirkungsgrad der Koagulation etwas erhohen

5. Gute der Abbildung

Die nach der Peripherie hin zunehmende Bildverschlechterung bei ophthalmoskopischer Beobachtung ist bekannt und wird durch die Strahlendurchrechnungen bestatigt Sie ist auch bei Verwendung des Kontaktglases noch wahrzunehmen allerdings erst bei wesentlich hoheren Werten des Gesichtswinkels (ungefahr ab 80°) Was fur die mit relativ kleinen Bundel Aperturen arbeitende Beobachtung gilt wirkt sich in noch wesentlich hoherem Masse fur Koagulationsbundel mit grosserer Apertur aus Bezuglich Bildgute sowohl der Beobachtung wie der Strahlenvereinigung des Koagulationsbundels wird also die Eindeilung gerade in der aussersten Peripherie von besonders hoher Wirkung sein was durch die Erfahrung bestatigt wird

Zusammenfassend kann gesagt werden dass das Ansteigen des Wirkungsgrades der Photokoagulation mit zunehmender Skleral Indentation aus klinischen Erfahrungen zwar bekannt ist Legt man sich jedoch die Frage vor wie die Koagulationstechnik weiter verbessert werden konnte so ist eine Kenntnis der einzelnen mitwirkenden Faktoren von einiger Bedeutung Es sollte hier versucht werden dazu in Bezug auf die Indentation einen Beitrag zu leisten

Die Zeichnungen stammen von Peter Schneider

Literatur

- 1 Cibis P L mitis and Hazards of Photocoagulation in Symposium on Photocoagulation Trans Amer Acad Ophthal and Otolaryng (6 71 87 (1967)
- 2 Cibis P L Ophthalmoscopy and other methods of examination in Controversial Aspects of the Management of Retinal Detachment Ed Schepens C L and Regan C D J Little Brown and Co (1965) pp 7 11
- 3 Farber F & Lotmar W Photocoagulation through the Goldmann Contact Lens Arch Ophthal 73 370 3 0 (1964)
- 4 Glimm H & Schmidt T Ein Kontaktglas zur Biomikroskopie der Ora serrata und der Pars Plana Ophthalmologica 149 481 483 (1964)
- 5 Eicher C Attachment for Goldmann Three mirror Contact Glass Amer J Ophthalmol 46 468 (1958)
- 6 Farber F Zusatztrichter zum Spiegel Kontaktglas mit verschieblichem Indentationsgrad Arch Ophthal 18 183 186 (1969)

3 Auftreffwinkel

Kurve (a) von Abb 5 stellt den Auftreffwinkel des Hauptstrahls auf der Netzhaut bei nicht eingedelltem Auge dar. Dieser Winkel beträgt zwar beispielsweise für einen Gesichtswinkel von 90° nur noch 38° jedoch ist die diesem Wert entsprechende Abnahme der Energiedichte eines auf die Netzhaut projizierten Koagulationsflecks nicht allzu drastisch nämlich rund 40 %. Durch Eindellung steigt der Auftreffwinkel wesentlich an (Kurve b) sodass namentlich gegen die äusserste Peripherie dieser Verlust nahezu vollständig aufgeholt werden kann.

Andererseits ist zu beachten dass bei schrägem Lichteinfall die Dicke der durchlaufenen Netzhautschichten verlängert erscheint. Die totale Absorption von Strahlung im Pigmentepithel welche für die Koagulationswirkung massgebend ist nimmt daher zu. Dieser Effekt kompensiert teilweise die oben besprochene Abnahme der Energiedichte. Im ganzen dürfte also die Grösse des Auftreffwinkels für die Photokoagulation eher von untergeordneter Bedeutung sein.

4 Kompression der Chorioidea

Wie Geeraets et al (12) gezeigt haben ist die Wärmeableitung aus dem Koagulationsfleck durch den Blutstrom in der Chorioidea für Pulszeiten unter $0,7$ sec zu vernachlässigen. Für die Koagulation mit gepulsten Laserquellen deren Pulsdauer in der Grössenordnung von 1 msec liegt spielt daher die Unterbin-

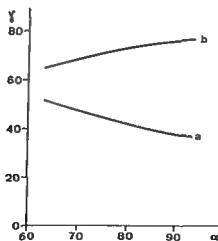


Abb 5

Auftreffwinkel γ in Funktion des Gesichtswinkels (a) ohne Eindellung (b) bei Eindellung der entsprechenden Netzhautstellen um 2,5 mm

SKLERALINDENTATION UND PERZEPTION

VON

F FANKHAUSER

I Einführung

Wir haben kürzlich den Prototyp eines Eindellungskontaktglases beschrieben (1) und (2) dessen Eindellungssporn sich bezüglich Länge und Inklination relativ zum Augapfel während der Beobachtung durch das Kontaktglas kontinuierlich verstellen lässt und das gestattet eine vom vordern Ende der Pars plana bis zum Äquator bulbi reichende Skleralindentation (SI) zu erzeugen.

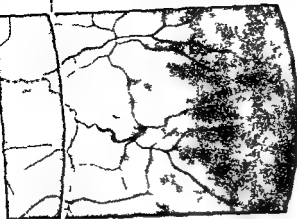
Es ist das Ziel der vorliegenden Arbeit die Wirkungsweise dieses Kontaktglases an zwei ausgewählten Fällen zu demonstrieren.

Im zweiten Teil dieser Arbeit werden wir uns mit den Schmechmechanismen beschäftigen die der Wahrnehmung und Erkennung in der Biomikroskopie im allgemeinen und der Indentations Biomikroskopie im speziellen zu Grunde liegen. Die Frage *warum* wir ein bestimmtes Phänomen beobachten ist von ebenso grosser Wichtigkeit wie die Beschreibung dessen *was* wir sehen. Nicht nur gewinnen wir dadurch einen Einblick in die optischen und biologischen Grundlagen des menschlichen Auges die der Perzeption zu Grunde liegen sondern wir werden in gleichem Masse zu apparativen Verbesserungen angeregt.

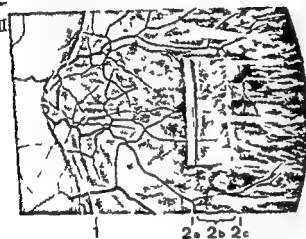
Eingegangen am 2. Juli 1969

This investigation was supported by a Grant to the University of Bern Number NB 03638 04 from the NINDS National Institutes of Health Bethesda Maryland U.S.A.

- 7 *Linder B* Photocoagulation after Fankhauser & Lotmar *Acta Ophthalmologica*, 48 86 90 (1960)
- 8 *Fankhauser F & Lotmar W* (1) A Contact Glass with adjustable Indentor *Hans Goldmann Festschrift Docum ophthal* 26 295 299 (1969)
- 9 *Lotmar W* A theoretical Eye Model with Aspherics In *Vorbereitung*
- 10 *Le Grand Y* *Optique Physiologique Tome premier Edition de la Revue d'Optique* (1952) p 12
- 11 *Jay B S* The effective pupillary area at varying perimetric angles *Vision Res.* 1 418 424 (1962)
- 12 *Gecraets W J et al* Rate of Blood Flow and its Effect on Chorioretinal Burns *Arch Ophthal* 68 58 61 (1962)



Figur 1
 Netzhautbezirk zwischen
 Aequator und Ora serrata
 I ohne Skleralindentation
 II mit Skleralindentation
 III Ora serrata näher
 Netzhautbezirk im Profil
 mit Skleralindentation
 Nähere Erläuterungen im
 Text.



I

II

Figur 2

Netzhautbezirk in der Gegend des Aequator bulbi I ohne Skleralindentation II mit Skleralindentation Nähere Erläuterungen im Text

II Das Eindellungskontaktglas in Aktion

Die Wirkung des neuen Kontaktglases soll an zwei Fällen mit verschiedener Schwierigkeitsgrad demonstriert werden. Fall 1 zeigt die Eindellungswirkung bei wenig komplizierten Verhältnissen. Den einzigen wesentlichen Störfaktor stellt hier vermehrtes Streulicht dar. Fall 2 zeigt ein Maximum an Komplexität und interpretativen Schwierigkeiten. Die zur Identifikation führenden Teilmechanismen sind aus dem Gesamteindruck oft nicht eindeutig isolierbar. In anderen Fällen scheint der dominante zur Wahrnehmung führende Wirkungsmechanismus in die Augen zu springen. Wo dies zutraf, wurde bei der Beschreibung der Fälle ausdrücklich darauf verwiesen. Da die Phänomene in Kapitel IV genauer erläutert sind, werden sie erst später wirklich verständlich werden.

Fall 1

Ein 57-jähriger Mann wurde am 4. 7. 1968 wegen einer beinahe totalen Amotio retinae os in die Augenklinik Bern aufgenommen. Eine genaue Untersuchung des Augenhintergrundes ergab verdächtige Stellen bei 11 h in Oranahe. Der Einblick war wegen einer geringfügigen Kerntrübung nicht besonders gut. Eine am 8. 7. 1968 durchgeführte Diathermokoagulation der verdächtigen Stellen sowie eine Umschlingung des Bulbus mit einem Skleraband und Ablassen der retroretinalen Flüssigkeit brachte eine sofortige Wiederanlegung. Die früher als verdächtig angesehenen Herde konnten nun mit Sicherheit als Ursache der Netzhautablosung eruiert werden, indem sich in deren unmittelbarer Umgebung anterior des Umschlingungsbandes etwas subretinale Flüssigkeit ansammelte. Die umschriebenen Flüssigkeitspolster wurden mit einer Photokoagulationsbarriere eingekreist. Schliesslich wurden Photokoagulate direkt auf die Läsionen gegeben.

Bei der Untersuchung des rechten Auges fand sich eine geringfügige bis massig stark entwickelte Kerntrübung. Bei stark schrägem Einblick storte das durch die Trübung erzeugte Streulicht deutlich. Das Gesichtsfeld betrachtet über den um 67° gegen die plane Vorderfläche geneigten Spiegel des Dreispiegelglases von Goldmann reichte bis in die Nähe der Ora serrata. Wir beschränken uns hier auf die Beschreibung eines schmalen Netzhautsektors bei 11 h, der ungefähr vom Äquator bis in die Nähe der Ora serrata reichte (Figur 1).

Die subjektive Beurteilung ohne SI ergab den Eindruck guter Bildscharfe in posterior-anteriorer Richtung bis zu einer bestimmten Stelle des Fundus zwischen Äquator und Ora serrata. An einem ziemlich gut definierten Punkt (1a) hatte man den Eindruck beginnender Bildunscharfe, die sich in anteriorer Richtung (Pfeil, Figur 1 I) verstärkte, wobei sich in diesem Gebiet die Strukturen zunehmend auflösten. Die Ora serrata ist in dem Bild nicht dargestellt. Sie

hervor (Optischer Schnitt der Retina bei III 5) Ein drittes Loch war im Profil mit dem inserierenden Glaskörper unter hohem Kontrast gegen den defokussierten dunkelblauen Hintergrund (III 4) sehr scharf erkennbar

Fall 9

Ein 56-jähriger Mann wurde am 26.6.1968 wegen einer Netzhautablosung mit Lochbildung rechts in die Augenklinik Bern eingewiesen. Die Netzhautablosung konnte mit Diathermie und einem eindellenden Eingriff geheilt werden. Am 27.11.1968 wurde der Patient mit einem Recidiv wieder aufgenommen, wobei sich die Ablosung auf den temporalen oberen und teilweise temporal unteren Quadranten beschränkte. Ein grosses Hufeisenloch wurde bei 11 h etwas posterior des Äquators gefunden; eine Gruppe mit kleineren Lochern fand sich bei 10 h, und bei 9 h wurde ein weiteres Hufeisenloch entdeckt. Die ganze Peripherie zeigte degenerative Veränderungen, auf die hier nicht näher eingegangen wird. Die Löcher wurden mit Diathermie getroffen; ferner wurde eine Skleratasche von 8.45 bis 11.15 h angelegt, deren Grund mit stumpfer Diathermie behandelt und schliesslich mit konservierter Sklera ausgestopft wurde. Im postoperativen Verlauf erfolgte prompte Wiederanlegung.

Am 5.8. und 10.10.1968 wurde die Umgebung des Loches bei 9 h mit dem Findellingskontaktilglas genauer untersucht. Dabei zeigten sich eine grosse Zahl von Störfaktoren, die die Erkennung wichtiger Einzelheiten stark behinderten.

Figur 1 gibt die Verhältnisse ohne, Figur 2 II die Situation mit Eindellung wieder.

Die Aufsicht auf die Figuren 1 und II (bis 2 rechter Bildrand) gibt den unverzerrten Eindruck wieder. Der Schnitt der Schichten bis und mit (5) ist in dem Sinne halbschematisch, als die natürlichen Proportionen nicht eingehalten wurden. Zwischen (4) und (5) wurden die tiefen Chorioidalgefässe, die (vom Atrophiebezirk unterhalb des Deckels abgesehen) nicht sichtbar waren, sinngemäss ergänzt. Der Lockdeckel ist bei (a) sichtbar. Das Loch selber ist nicht mehr sichtbar und ist durch reaktive Pigmentproliferationen verdeckt. Links unterhalb des Deckels beobachtete man die oben erwähnte atrophische Zone, in der nur einige Chorioidalgefässe erhalten sind. Weiter findet sich eine Blutung bei (b), die im optischen Schnitt in die Retina lokalisiert werden konnte. Daran schliesst sich eine atrophische Zone (c) mit lockerer Ausstreuerung von polymorphem Pigment an, das ebenfalls intraretinal liegt. Es folgt nach unten ein Gebiet, das durch eine unregelmässige Oberfläche charakterisiert ist (d). Die streifigen Oberflächenirregularitäten (die einen weiss-rotlichen Farbton hatten) waren gegen das atrophische Gebiet ausgerichtet, was auf Zug

darf bei etwa (3) der Figur 1 I und II angenommen werden Ueber allen Area len hatte man den Eindruck uniformer und homogener Dicke und Verteilung des Pigmentepithels Die Netzhautoberfläche war regelmässig (glatter Oberflächenstreifen 1) Die Einfallsrichtung des Beleuchtungsbündels ist in Figur 1 durch einen dicken horizontalen Pfeil angedeutet Figur 1 II gibt die gleichen Abschnitte bei Eindellung wieder Diese ging so vor sich dass der Eindellungsdorn mit zunehmender Steilheit relativ zur optischen Achse gegen posterior verschoben wurde Diese verschiedenen Eindellungspositionen wurden in der Figur in einen Eindruck verarbeitet wobei der Eindellungsdorn in seiner Endposition dargestellt ist Das Eindellungsbild der an die Ora serrata angrenzenden Netzhaut ist in Figur 1 III dargestellt Die Eindellungsbilder 1 II und III ergaben foldende wesentlichen Unterschiede relativ zu Figur 1 I

1 Ueber dem *ganzen* einsehbaren Gebiet herrschte der subjektive Eindruck der Bildscharfe

2 Die Abblassung des I undusrot über dem Eindellungsgebiet war ausgesprochen Das Rot hatte einem gelblichen Farbton Platz gemacht Die grossen Chorioidalgefässe waren noch sichtbar Sie erschienen verdunnt und der sie auszeichnende rote Farbton relativ zu I entsättigt

3 Gegen den abgeblassten Hintergrund trat Struktur und Verteilung des chorioidalen Pigmentes ausserordentlich deutlich hervor und feinste Pigmentkornner konnten ohne Schwierigkeiten erkannt werden Aus Figur I hatte man geschlossen dass sich das chorioidale Pigment homogen auf die Intervaskularen Bezirke verteile

Es ist mit grosser Wahrscheinlichkeit anzunehmen dass die Verbesserung des Auflösungsvermögens durch eine Verbesserung der Bildqualität und durch eine Umwandlung der Farbkontraste in Schwarz Weiss Kontraste infolge Kompression der Chorioidea zu Stande kam

4 Die Glaskörperstruktur im retrolentalen Raum (2b) war leicht beurteilbar ebenso wie die Insertion der Glaskörperbasis an der Retina die einzelne feine Verdickungen an der Netzhautoberfläche zeigte (2c) die sich als feine Streifen gegen die Ora serrata fortsetzten (2a deutet den Linsenrand mit dem Abspaltungsstreifen an)

5 Bemerkenswerterweise erschienen die typische chorioidale Pigmentstruktur und feinste Netzhautgefässe nun auch in der Zone die ohne SI (Figur 1) als subjektiv scharf jedoch als homogen und frei von feinsten Netzhautgefässen beurteilt worden war

Subjektive Bildscharfe ist somit kein zuverlässiges Kriterium für das Auflösungsvermögen

6 Die an die Ora serrata angrenzende Retina erschien in III völlig scharf Ihre Farbe war in Schragprojektion grau weiss wobei das Pigment der Chorioidea körnig durchschimmerte Gegen den nicht eingedellten rothlichen Hintergrund traten in den ausgedehnten Blessig Iwanowschen Cysten zwei ovale Locher

III Wahrnehmung Erkennung und Identifikation in der Biomikroskopie

Wahrnehmung ist bekanntlich eine notwendige aber nicht hinreichende Voraussetzung zur Erkennung und Identifikation einer bestimmten Struktur. Wir werden diese beiden Prozesse aus diesem Grunde getrennt behandeln.

1 Wahrnehmung in der Biomikroskopie

Man darf als allgemein bekannt voraussetzen, dass die Sichtbarkeit eines stationären Objektes von der Helligkeit des Hintergrundes, auf dem es erscheint, von seiner Form, seiner angularen Grösse, ferner von seinem Helligkeits- und Farbkontrast abhängt.

Allgemein gilt: je grösser die Helligkeitsdifferenz zwischen Objekt und Hintergrund ist, umso besser wird das Objekt wahrgenommen, wobei wir hier einen unformen Hintergrund voraussetzen.

Diese Aussage lässt sich auf mikroskopische Bilder übertragen. Da alle Dimensionen eines Objektes linear vergrössert werden, hängt die durch das Mikroskop wahrgenommene Fläche eines Objektes A' mit der Vergrösserung M und der wirklichen Fläche A des Objektes durch die Beziehung

$$A' = A \cdot M^2 \quad (1)$$

zusammen

kleine nicht sichtbare Objekte können somit, wenn sie geeignet vergrössert werden, durch Helligkeitssummation wahrgenommen werden.

Die durch die Vergrösserung bedingte Verbesserung der Wahrnehmung erreicht in der Biomikroskopie jedoch sehr bald einen Grenzwert: der erfahrungsgemäss bei klaren Medien etwa bei einer 20-fachen Vergrösserung liegt. Stärkere Vergrösserungen bringen infolge der durch Vibrationen erzeugten Bildunschärfe und der zunehmenden Gesichtsfeldverengung im allgemeinen keinen Gewinn. Sind die Medien trübe, so wird die Vergrösserung in dem Masse weniger wirksam, als die Turbidität der Medien zunimmt.

Es ist wichtig zu wissen, dass die Sichtbarkeit von Objekten gleichen Flächeninhaltes für kreisförmige Objekte immer am besten ist (3) und (4). Der wichtigste Faktor, der die Sichtbarkeit beeinflusst, ist der durch den Beobachter wahrgenommene scheinbare Bildkontrast C . Dieser setzt sich aus zwei Komponenten zusammen: Die eine ist der scheinbare Helligkeitskontrast C_h , und die andere der scheinbare Farbkontrast C_c , die bei der Erkennung von farbigen Objekten stets zusammenwirken. Der Beitrag von C_{ca} und C_b für die Erkennung nimmt die allgemeine Form an

$$C = (C_h^2 + C_c^2) \quad (2)$$

wirkung durch das Narbenareal schliessen lässt Diese Interpretation wird da durch gestützt dass durch SI (Änderung der Spannungsverteilung in der Retina) die Irregularitäten ihre Ausrichtung verloren und einer unregelmässigen hockerigen Oberfläche Platz machten (Figur 2 II) Ohne Eindellung waren die Netzhautunebenheiten wegen der durch die Ueberlagerung mit polymorphen Glaskörpertrübungen erzeugten Tarnung nicht erkennbar Durch Hin und Herbewegen des Dornes wurden die Glaskörpertrübungen und die Netzhautirregularitäten sowie die darunter liegenden Strukturen als schichtweise angeordnete separate Strukturen unterscheidbar Die Erkennung erfolgte hier offensichtlich auf Grund der durch den Dorn induzierten Bewegungsperspektive Im Streifen (1) bis (1) ist durch den Künstler versucht worden die Störung der Glaskörpertrübungen auf die darunterliegenden Strukturen darzustellen Ueber den übrigen Bildpartien wurde der getrübe Glaskörper mit seinen Opazitäten weggelassen (1) zeigt den optischen Schnitt durch den Glaskörper (2) den Schnitt durch die Retina Man erkennt dass die faserigen und klumpigen Elemente kurz vor der Netzhaut an einer wenig scharfen Membran enden die in der unteren Hälfte der Figuren 2 I und II feine Faserzüge zur Netzhaut sendet

In Figur 2 I sieht man dass von den oberflächlichen Chorioidalgefässen nur diejenigen deutlich hervortreten die perpendicular oder in einem grossen Winkel gegen die Streifenzeichnung der Netzhaut verlaufen Parallel zur Streifenzeichnung laufende Chorioidalgefässe sind nur mit grosser Mühe erkennbar Eine Deutungsmöglichkeit für dieses Phaenomen besteht darin dass der Tarn effekt einer überlagernden Struktur bei paralleler Ausrichtung zur überlagerten Struktur viel ausgeprägter sein kann

Die genaue Konfiguration der Oberflächenirregularitäten wird im Profil durch SI in Figur 2 II deutlich Bei der Indentationsbedingten seitlichen Betrachtungsrichtung nimmt die Retina durch Vergrösserung der scheinbaren Schichtdicke einen grauen Ton an und es gelingt ein System bestehend aus hochgradig verdünnten Stellen auszumachen (e) die sobald der Eindellungsdruck etwas nachlässt sofort ausgesprochen rot gegen die graue Netzhaut erscheinen Der Schnitt mit dem dünnen optischen Spalt (2) zeigt durch Spalttransposition dass die drei Verdünnungen am unteren Bildrand bereits durchgerissen sind und Locher darstellen Man beachte die drei zusammenhängenden Deckel die sich auf die Netzhautoberfläche geklappt haben Wenn wir die Figuren 2 I und II miteinander vergleichen wird es offensichtlich dass wir die drei Locher wegen der ungünstigen Beobachtungsbedingungen ohne Eindellung übersehen hatten

Schicht (2) bis (3) zeigt die Retina und Schicht (3) bis (5) die Chorioidea im optischen Schnitt Die Vernarbungen im oberen Teil des Bildes in der Nähe der Deckelinsertion wurden blaulich wiedergegeben da sie im kurzwelligen Blaulicht blaulich weisslich fluoreszierten

Bei extrem schragem Strahlengang nimmt die CR sehr niedrige Werte an. Durch den Einsatz des Kontaktglases wird die CR jedoch wieder angehoben wie früher auseinander gesetzt worden ist (1)

SI führt zu einer weiteren Verbesserung der CR indem das eingedellte Netz hautareal gegen die optische Achse zu verschoben und dort unter einem kleineren Gesichtswinkel mit einer besseren CR beobachtet werden kann.

Die Anwendung des Kontaktglases und SI führen somit synergistisch zu einer Erhöhung der scheinbaren Helligkeits- und Farbkontraste.

Andererseits führt Streulicht zu einer Reduktion der scheinbaren Kontraste und damit zu einem Abfall der CR.

2. Verminderung des Streulichtes durch SI

Die Verminderung des Streulichtes im Beobachtungssystem und damit die Verbesserung der Bildqualität kann auf zwei Arten zustandekommen

a) Durch die Eindellung wird die kleine Achse der in Schragprojektion elliptisch deformierten Pupille infolge des verminderten Gesichtswinkels effektiv vergrößert. Bei der Beobachtung der seitlichen Fundusabschnitte fallen der Beobachtungsstrahl sowie der Beleuchtungsstrahl (bei monokularen Instrumenten) oder die beiden Beobachtungsstrahlen sowie der Beleuchtungsstrahl (bei binokularen stereoskopischen Instrumenten) in die kleine Achse der elliptisch deformierten Pupille. Wir wissen, dass das in das Beobachtungssystem rückgestrahlte Streulicht in dem Masse abnimmt, als es uns gelingt, den Beleuchtungs- und Beobachtungsstrahlengang in der Pupille und den Medien zu trennen.

Dies wird bei einigen Instrumenten durch Anlage des Beleuchtungssystems in der Art erreicht, dass der Beleuchtungsstrahl über oder unter die beiden Beobachtungsstrahlen zu liegen kommt. Bei einem in der Pupille frei verschiebbaren Beleuchtungsstrahl der Instrumente dieser Klasse wird dieser in der grossen Achse der elliptisch deformierten Pupille und so weit wie möglich von den Beobachtungsstrahlen weggeschoben.

Wenn die apparativen Voraussetzungen für die Verschiebbarkeit des Beleuchtungsstrahles fehlen, so wird die Voraussetzung für eine bessere räumliche Trennung durch die Eindellung dadurch geschaffen, dass der kleine Pupillendurchmesser effektiv vergrößert wird. Eine quantitative Abschätzung dieses Effektes wurde an anderer Stelle gegeben (2).

b) Von der Vergrößerung des nutzbaren Pupillendurchmessers abgesehen ist zu beachten, dass durch die Eindellung die betreffende Netzhautpartie nicht nur gegen das Rotationszentrum des Auges verschoben wird, eine Komponente der Eindellrichtung ist gegen die Pupille gerichtet, wodurch der optische Weg des Beobachtungs- und Beleuchtungsstrahles im Auge abnimmt. Bei starker Turbidität wird durch diese Verminderung der Schichtdicke und die damit ver-

Sobald der scheinbare Kontrast C_a unter einen kritischen Wert sinkt der durch die Kontrastempfindlichkeit des Beobachters gegeben ist wird das Objekt nicht mehr wahrgenommen

Zur Beurteilung der Wahrnehmbarkeit eines Objektes braucht jetzt nur noch der Zusammenhang zwischen dem scheinbaren Kontrast C_a und dem Objektkontrast C_o hergestellt zu werden

Dieser Zusammenhang wird durch die Formel (3) gegeben

$$CR = C_a \cdot 100/C_o \quad (3)$$

worin CR die Kontrastrendite in Prozent bedeutet Die CR ist ein Mass für die Güte eines gegebenen optischen Systems

2 Erkennung und Identifikation

Die Erkennung und Identifikation bestimmter Strukturen in der Biomikroskopie wird in vielen Fällen nicht so sehr dadurch erschwert dass Strukturen als ganze oder in Strukturen eingebettete Einzelobjekte nicht wahrgenommen werden sondern dadurch dass sie in einer komplexen Umgebung liegen in der sie nicht erkannt werden und durch Tarnung verschwinden Die sich überlagern den Schichten der Netzhaut und Aderhaut und oft auch des Glaskorpers die wieder aus zahlreichen Einzelelementen bestehen bilden einen Hintergrund der aus multiplen sich überschneidenden Strukturelementen besteht und die Identifikation pathologischer Veränderungen in vielen Fällen erschwert oder verunmöglicht

Es ist wohlbekannt dass die Wahrscheinlichkeit ein Einzelobjekt als solches zu erkennen in dem Masse abnimmt als die Gesamtheit der nicht relevanten das Objekt einbettenden übrigen Strukturelemente zusammengedrängt wird (5) (6) und (7) Die Erfahrung lehrt dass bei diagnostischen Schwierigkeiten die auf diesem Tarneffekt beruhen durch SI oft Erkennung möglich ist

IV Die Wirkungsweise der Skleralindentation

Die Wirkung der SI besteht darin die optischen Voraussetzungen im unbetrübten Auge so zu verändern dass die Erkennung und/oder Wahrnehmung schwer erkennbarer Strukturen verbessert oder überhaupt erst möglich wird

1 Das Zusammenwirken von SI und Kontaktglas Biomikroskopie

Das dioptrische System des Auges ist dadurch charakterisiert dass die CR umso mehr abnimmt je schräger das System vom Strahlengang durchlaufen wird

Bei extrem schragem Strahlengang nimmt die CR sehr niedrige Werte an. Durch den Einsatz des Kontaktglases wird die CR jedoch wieder angehoben wie früher auseinandergesetzt worden ist (1).

SI führt zu einer weiteren Verbesserung der CR, indem das eingedellte Netz hautareal gegen die optische Achse zu verschoben und dort unter einem kleineren Gesichtswinkel mit einer besseren CR beobachtet werden kann.

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knüpfte Verminderung des Streulichtes im Beobachtungssystem die schlecht oder überhaupt nicht mehr sichtbare Retina oft wieder in deutliche Schdistanz gerückt

3 Die optischen Auswirkungen der Aenderung des Auftreffwinkels des Beobachtungs und Beleuchtungsstrahles durch SI

Durch die Eindellung kommt es notwendigerweise zu einer Aenderung des Auftreffwinkels des Beobachtungs und Beleuchtungsstrahles hinsichtlich der beobachteten Netzhautregion wobei wir unter Auftreffwinkel den Winkel verstehen den der Beobachtungs- oder Beleuchtungsstrahl mit der in der Auftreffstelle an den Augapfel gelegten Tangente bildet Wir haben an einer anderen Stelle die Variation des Auftreffwinkels in Abhängigkeit vom Gesichtswinkel des einfallenden Strahlenbündels für eine vorgegebene Eindelltiefe angegeben (2) Durch die Beobachtung unter schiefer Inzidenz werden die Strukturen perspektivisch verzerrt und machen eine Reihe von Formtransformationen durch Es ist eine einleuchtende Erfahrungstatsache dass die Erkennung und Identifikation pathologischer Stellen oft in einer ihrer Transformationsformen besonders leicht ist und die Struktur dann als besonders typisch erscheint Es ist ferner zu beachten dass die scheinbare Schichtdicke und damit die Transparenz der durchstrahlten semitransparenten Schichten vom Auftreffwinkel des Beobachtungsbündels abhängt Wie jedem Biomikroskopisten bekannt ist macht sich die durch den Beobachtungsstrahl senkrecht getroffene Netzhaut je nach dem beobachteten Netzhautareal als kaum wahrnehmbare (Peripherie) oder deutliche Verschleierung (Papillennahe) der darunter liegenden Chorioidea bemerkbar Bei kleinen Auftreffwinkeln des Beobachtungsbündels erscheint selbst in Ora serrata Nahe die Netzhaut opak Damit müssen aber auch die scheinbaren Kontraste der Strukturelemente die in der Netzhaut und Aderhaut eingelagert sind variieren

Die durch Variation des Auftreffwinkels des Beobachtungsstrahles erzeugten Veränderungen des Farbtones und der Sättigung eines betrachteten Netzhautareals werden aus dem Gesagten verständlich

Die Aenderung der Differenz des Auftreffwinkels von Beleuchtungs und Beobachtungsbündel ist ein wichtiges diagnostisches Hilfsmittel da dadurch die Schichtdicke des optischen Schnittes kontrolliert wird Die letztere sollte nicht mit der erwähnten scheinbaren Schichtdicke verwechselt werden Die Schichtdicke des optischen Schnittes ist die in der Strahlrichtung gemessene Dicke des durch das Beleuchtungsbündel herausgeschnittenen durch Streulicht sichtbaren Gewebsschnittes

Es ist bekannt dass die Tiefenlokalisation und damit die räumliche Zuordnung zur Schicht in der ein Strukturelement liegt umso leichter ist je grösser die scheinbare Schichtdicke gewählt wird Daraus folgt die Regel dass der

Winkel zwischen Beobachtungs- und Beleuchtungsbündel so gross wie möglich gewählt werden sollte

Optimale Beobachtungsbedingungen werden erfahrungsgemäss in vielen Fällen durch die Inspektion eines Strukturelementes im Profil erzielt. Durch Verschiebung des Strukturelementes auf die Höhe des Eindellungswalles wird das durch den Beleuchtungsstrahl getroffene Detail gegen einen entfernten defokussierten und damit dunklen und homogenen Hintergrund unter einem hohen scheinbaren Kontrast wahrgenommen.

Wie in III (1) und III (2) auseinandergesetzt wurde, verbessern die bei der Profilbetrachtung zur Auswirkung kommende Vergrösserung des scheinbaren Kontrastes und die Vertauschung eines komplexen gegen einen homogenen Hintergrund die Sichtbarkeit eines schlecht erkennbaren Strukturelementes oft sehr stark. Die Inspektion einer suspekten Netzhautregion bei verschiedenen Graden der Eindelltiefe erweitert somit eindeutig unsere diagnostischen Möglichkeiten.

4 Die Bedeutung parallaktischer Bewegungen für die Strukturerkennung

Es ist von grosser Wichtigkeit, nicht nur statische Zustände wie wir sie in Kapitel IV 3 beschrieben haben, zu betrachten, sondern ein bestimmtes kritisches Netzhautareal zu beobachten, währenddem der Eindellungsdorn hin und her bewegt wird. Eisner (8) hat unseres Wissens als erster auf den Wert dieser Untersuchungsmethode aufmerksam gemacht. Da der Unterschied im Parallaxwinkel zwischen Netzhaut und Chorioidea unter normalen Bedingungen zu gering ist, wird hier bei Verschiebungen einer Fundusstelle durch den Eindellungsdorn meist keine parallaktische Bewegung der Schichten gegeneinander wahrgenommen.

Unter pathologischen Bedingungen, zum Beispiel beim Vergleich von geformten präretinalen Corporustrübungen mit retinalen Strukturen bei der Gegenüberstellung von aufstehenden Lochrändern mit ähnlichen Strukturmustern der Retina und Chorioidea, bewegen sich die in verschiedener Tiefe gelegenen Elemente und Verbände mit unterschiedlicher Winkelgeschwindigkeit, sobald eingedellt wird, und können dadurch bedeutend leichter voneinander unterschieden werden. Es ist gezeigt worden (9), dass die Bewegungsperspektive nicht nur die Tiefenlokalisation einzelner Strukturelemente erleichtert oder überhaupt erst ermöglicht, vielmehr werden zerstreute Einzelelemente eines Strukturverbandes, deren Zusammengehörigkeit zu erkennen unter statischen Bedingungen nicht möglich ist, durch die Bewegungsperspektive zu einem einheitlichen Ganzen zusammengeschlossen. Dieser Mechanismus wird von den Gestaltpsychologen als *common fate* bezeichnet. Auf Grund dieses Phänomens gelingt es oft, die Zusammengehörigkeit schichtweise angeordneter, regelloser und lockerer Strukturen und damit von Schichtgrenzen zu erkennen.

5 Die Verbesserung der Perzeption durch Kompression der Chorioidea

Die Chorioidea wirkt bekanntlich wie ein Rotfilter wobei sie durch das Beleuchtungsbündel zweimal durchlaufen wird. Die genauesten Untersuchungen über die spektralen Eigenschaften der Chorioidea scheinen von Geeraets et al (10) zu stammen. Es ist offensichtlich, dass das spektrale Verhalten der Chorioidea nicht mit einer Blutschicht von äquivalenter Schichtdicke übereinstimmt. Man kann jedoch annehmen, dass bei zunehmender Kompression der Chorioidalgefäße die Absorptionskurve der Chorioidea angenähert so verändert wird, als ob von der Gesamtabsorptionskurve der Chorioidea im gefüllten Zustande die Absorptionskurve einer Blutschicht von zunehmender Schichtdicke subtrahiert wurde. Prince (11) hat die Absorptionskurve für Blutschichten variabler Dicke bekanntgegeben. Die Chorioidea schneidet somit aus dem Emmissionsband der Beleuchtungsquelle je nach Schichtdicke wichtige Anteile heraus und kann dadurch als Störfaktor wirken. Bei der SI steigt durch Ausschaltung der Filterwirkung der Chorioidea die Intensität des von der Sklera rückgestrahlten Lichtes und zwar vor allem im Grün und Blau für welche das Sehorgan empfindlicher ist. Damit wird das Pigment gegen einen helleren weißen Hintergrund unter verstärktem Kontrast wahrgenommen. An dieser Kontraststeigerung ist indessen auch die Verbesserung der Abbildungsgüte durch Reduktion des Gesichtswinkels in geringerem oder stärkerem Masse beteiligt wie in (2) auseinandergesetzt wurde.

Die Kontrasttransformation ist aber nicht vollständig, da einerseits wohl nie eine völlige Kompression der Chorioidalgefäße gelingt, andererseits stets ein Anteil des eingestrahlten weißen Beleuchtungslichtes spektral unverändert im rückgestrahlten Licht (12). Trotz dieser Restriktionen wirkt sich die Kontrastverstärkung und die Verbesserung der Sichtbarkeit wichtiger Strukturelemente in der Biomikroskopie klar und überzeugend aus wie im Fall 1 gezeigt wird.

Ohne Zweifel kann das chorioidale Rotlicht durch geeignete Sperrfilter (so genannte Rotfreifilter) im Beleuchtungs- oder Beobachtungsstrahlengang eliminiert werden, die aber zwangsläufig ihrerseits wiederum spektrale Restriktionen einführen, eine Beobachtung des Fundus im polychromatischen Licht unmöglich machen und damit zu einem Informationsverlust führen. Wir haben wiederholt beobachtet, dass die Kompression der Chorioidea wirkungsvoller ist als jede Manipulation mit spektral selektiven Filtern, um bestimmte Strukturelemente der Retina und Chorioidea zur Darstellung zu bringen.

6 Die Auswirkung besonderer Untersuchungsbedingungen auf die Perzeption in der Biomikroskopie

Wir schildern in folgenden einige Effekte, deren Erklärung umstritten ist und die auch noch andere Deutungsmöglichkeiten zulassen.

Es geht uns in erster Linie darum, anzuregen, dass alle apparativen Möglich-

keiten ausgeschöpft werden. Es ist oft auffallend, dass die Erkennbarkeit von Struktureinheiten von deren Orientierung abhängt, d.h. ob sie waagrecht, schrag oder senkrecht im Bildfeld erscheinen. Dies setzt natürlich voraus, dass die beobachtete Struktur eine oder mehrere Symmetrieachsen besitzt. Takala (13) hat gezeigt, dass die Komponenten komplexer Figuren, die eine vertikale Symmetrieachse besitzen, besser erkannt werden. Fitts et al. (14) gelangten zum selben Schluss. Ein einfaches Mittel, um die Orientierung beobachteter Strukturen zu ändern, das aber nur eine begrenzte Wirkung hat, besteht in der Rotation des Spiegels des Goldmann-Glases. Da die Spiegel ausreichend gross sind, kann in vielen Fällen das Kontaktglas beträchtlich gedreht und damit die Orientierung der beobachteten Struktur geändert werden, bis das beobachtete Netzhautareal aus dem Gesichtsfeld hinauswandert.

Die relative Orientierung der Grenzen des ausgeleuchteten Beobachtungsfeldes oder Beobachtungsspaltens zu der beobachteten Struktur ist nicht irrelevant. Auch hier muss offensichtlich das Vorhandensein einer oder mehrerer Symmetrieachsen gefordert werden, damit das Phänomen zur Beobachtung kommt.

Je nach Ausrichtung der Struktur zu den Grenzen des überlagerten Lichtspaltens oder des Lichtstreifens kann diese besser oder weniger gut erkannt werden. Hopfermann (15) hat auf diese Zusammenhänge aufmerksam gemacht und sie näher untersucht. Wir haben es in der Hand, den Spalt oder den Lichtstreifen je nach der Strukturorientierung auszurichten und zu prüfen, ob in dem betrachteten Falle eine Verbesserung der Erkennbarkeit eintritt oder nicht.

Wir sind Adelheid Meyer für die Ausführung der Funduszeichnungen zu grossem Dank verpflichtet.

Literatur

- 1 Finkelstein F & Littman W A. Contact Glass with an adjustable Indentor. Hans Goldmann Festschrift. Article Documenta Ophthalmologica 26: 295-299, 1969.
- 2 Finkelstein F & Littman W. Skleralindentation und Photocoagulation. Acta Ophthalmologica 49: 252-259, 1970.
- 3 Koffman A B & Blackwell H R. Effects of Target Size and Shape on Visual Detection. J Opt Soc Am 47: 114, 1957.
- 4 Koffman A B. Visual Detection as Influenced by Target Form in Form Discrimination as related to military Problems. p. 109. Publ. 561. National Academy of Sciences National Research Council, Washington D.C.
- 5 Koffman A B & Bush W R. Laboratory Studies pertaining to visual air reconnaissance. USAF Wright Air Development Center, Wright Patterson AFB, Ohio. Tech. Rept. 55, Part I and Part II, 1961.

- 6 Boynton R M & Bush W R Recognition of Form against a Complex Background
J Opt Soc Am 46 758 1956
- 7 Boynton R M Recognition of critical targets among irrelevant forms in Form
Discrimination as related to Military Problems p 175 Publ 561 National Ac. of
Sciences National Research Council Washington, D C
- 8 Eisner G Zur Spaltlampenmikroskopie der Ora serrata und Pars plana corporis
ciliaris I Mitteilung Graefes Arch Ophthal 176 223 1968
- 9 Gibson J J The Perception of the Visual World Chapter 7 Houghton Mifflin ed
Boston 1950
- 10 Geerarts W J et al The relative absorption of thermal energy in Retina and
Choroid Invest Ophthal 1 340 1962
- 11 Prince J H Spectral Absorption of the Retina and Choroid from 340 1,00 mil
limicrons Publication 14 Institute for Research in Vision Ohio State University
Ohio USA 1962
- 12 Alpern M & Campbell F W The Spectral Sensitivity of the Consensual Light
Reflex J Physiol 104 478 1962
- 13 Takala M Asymmetries of the Visual Space Ann Acad Sci fenn 17 180 501
313 314 1951
- 14 Fitts P M et al Stimulus Correlates of Visual Pattern Recognition a Probability
Approach J Exp Psychol 51 1 1956
- 15 Kopfermann H Psychologische Untersuchungen über die Wirkung zweidimensio
naler Darstellungen körperlicher Gebilde Psycholog Forschung 13 293 1950

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BY

LENNART BERGGREN

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In vivo and *in vitro* mercury inhibits cation transport in the kidney (9). It prevents the active uptake of sodium and potassium from the medium in the Crustacean *Daphnia Magna* (14) and inhibits the sodium transport in the frog skin (17).

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The action of mercury on active cation transport made it of interest to investigate if the drug could influence *in vitro* secretory activity of the ciliary processes of the eye.

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Male albino rabbits weighing about 2 kg and fed a diet of hay and oats and water ad lib were used.

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- 7 Boynton R M Recognition of critical targets among irrelevant forms, in Form
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- 9 Gibson J J The Perception of the Visual World Chapter 7 Houghton Mifflin ed
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- 10 Geercks W J et al The relative absorption of thermal energy in Retina and
Choroid Invest Ophthal 1 340 1962
- 11 Prince J H Spectral Absorption of the Retina and Choroid from 340 to 1000 m μ
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- 12 Alpern M & Campbell F W The Spectral Sensitivity of the Consensual Light
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- 13 Takala M Asymmetries of the Visual Space Ann Acad Sci Fenn 190 301
313 314 1951
- 14 Fitts P M et al Stimulus Correlates of Visual Pattern Recognition a Probabilistic
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- 15 Kopfermann H Psychologische Untersuchungen über die Wirkung zweidimensio-
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Secretory pumping *in vitro* has been described in detail previously (3,4). The gradual shrinkage in size that the ciliary processes show on incubation in a physiologic buffer solution was taken as a measure of secretory activity. The tissue fluid of the ciliary processes was replaced with a physiologic buffer solution by perfusion through a carotid artery in the living animal. Sections of iris ciliary body were prepared and put into a bath containing the same buffer solution. Care was taken to prevent secretion as much as possible up to the incubation *in vitro*. The area of a transverse optical section of the processes was photographed intermittently for one hour and one to four processes were generally suitable for planimetry. The reduction in area of the different processes was calculated in per cent from the zero time value and averaged for each time. The single eye was treated as the statistical unit. Ciliary processes showing a shrinkage of 1 per cent or less at 5 minutes were considered to have impaired function. Those with a shrinkage of 15 per cent or more at 5 minutes were assumed to have too small a residual capacity. In control experiments the processes shrink down to about 65 per cent of the zero time value in one hour. The minimum slope line is defined as a straight line from the point of 85 per cent remaining surface area at 5 minutes from zero time to the mean value plus 3 standard deviations at 60 minutes. Blocking effects on secretion were considered to have occurred if the curves of shrinkage after the addition of drugs (always at plus 5 min) were above the minimum slope line. This criterion allows relatively small samples to be used.

Mersalyl injections *in vivo* In order to investigate if mersalyl injected *in vivo* might have any effect on secretory pumping of the ciliary processes *in vitro* without mersalyl in the bathing medium the following experiments were performed. Six rabbits were given 1 ml of mersalyl intramuscularly on two consecutive days. *In vitro* experiments of secretory pumping were done on three rabbits one hour after the last injection and on three rabbits one day after the last injection. Because no drug is added to the bathing medium a slightly different standard curve is used as described previously (4).

Drugs

Buffer solution The physiological buffer solution was made up as described previously (4) and prepared from chemicals of analytical grade. With the concentrations expressed in mM/L the composition was NaCl 150 KCL 3 MgSO₄ 7 H₂O 1 glucose. The solution was tris buffered and equilibrated with 95 per cent O₂ 5 per cent CO₂ to a pH of 7.4.

Mersalyl Mersalyl® (ACO Sweden) Ampoules of 2 ml containing 100 mg mersalyl and 50 mg theophylline per ml. Mersalyl mol w 506 Theophylline mol w 180.

Theophylline Teofyllamin® (ACO Sweden) Ampoules of 2 ml containing 100 mg theophylline per ml. Theophylline mol w 180.

Dimercaprol BAL (Boots Pure Drug Co Ltd England) Only injection of dimerca

prol 0.05 g dimercaprol/ml of arachis oil containing 10% benzyl benzoate Ampoules of 2 ml Dime caprol mol w 124

Results

Mersalyl in the bathing medium Mersalyl caused a pronounced effect on secretory pumping. In the final part of the experiment the area of the ciliary processes increased when a concentration of mersalyl from 0.1 mg/ml was used. A concentration of 0.2 mg/ml (4×10^{-4} M) resulted in an increase at 60 min up to 116 per cent of the zero time value. A concentration of 0.01 mg/ml was without effect (Fig. 1).

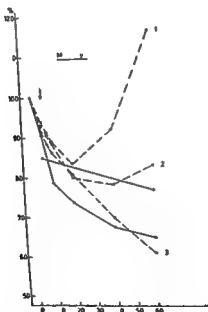


Fig. 1

Mersalyl added to the bathing solution at arrow. Ordinate = calculation of transverse section area of ciliary processes in per cent. Zero value = 100 per cent. Abscissa = time in minutes. Mean selected time shrinkage curves. Curve 1 = 0.2 mg/ml mersalyl (4×10^{-4} M) (5 animals, 12 processes). Curve 2 = 0.1 mg/ml mersalyl (5 animals, 7 processes). Curve 3 = 0.01 mg/ml mersalyl (5 animals, 11 processes). Continuous curve = mean selected standard curve with buffer solution, pH 7.4. Minimum slope line from 85 per cent at 5 minutes to mean standard value plus three standard deviations at 60 minutes.

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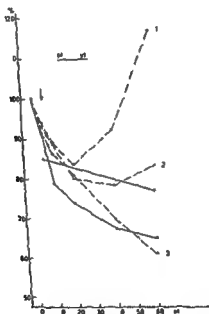


Fig 1

Mersalyl added to the bathing solution at arrow. Ordinate = calculation of transverse section area of ciliary processes in per cent. Zero value = 100 per cent. Abscissa = time in minutes. Mean selected time shrinkage curves. Curve 1 = 0.2 mg/ml mersalyl, 4×10^{-4} M (> 30 animals, 1 process). Curve 2 = 0.1 mg/ml mersalyl (> 30 animals, 7 processes). Curve 3 = 0.01 mg/ml mersalyl (5 animals, 11 processes). Continuous curve is an selected standard curve with buffer solution pH 7.4. Minimum slope line from 85 per cent at 5 minutes to mean standard value plus three standard deviations at 60 minutes.

Mersalyl® solution contains theophylline. The final concentration in the bathing medium was 0.1 mg/ml of theophylline when the highest concentration of mersalyl (= 0.2 mg/ml) was used. Experiments with theophylline only, using a tenfold concentration i.e. 1.0 mg/ml, was without effect on the normal shrinkage of the ciliary processes (fig. 2).

Dimercaprol BAL was without effect on the normal shrinkage of the ciliary processes in a final concentration of 4×10^{-4} M. The effect of mersalyl could be blocked by an equimolar concentration of BAL (BAL 4×10^{-4} M and mersalyl 4×10^{-4} M) (fig. 2).

Mersalyl injections in vivo. After mersalyl injections *in vivo* the succeeding *in vitro* experiments without any drug in the bathing medium did not show any effect on secretory pumping differing from normal conditions. The two groups were similar. The first group had a mean value at 60 min of 55.6 per cent (3 animals, 9 processes) and the second group a mean value at 60 min of 53.2 per cent (3 animals, 7 processes). The combined group is recorded in fig. 3.

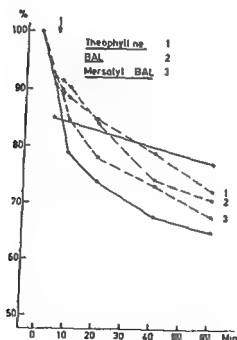


Fig. 2

Theophylline, dimercaprol BAL and theophylline plus dimercaprol BAL added to the bathing solution at arrow. Coordinates as in fig. 1. Mean selected time shrinkage curves. Curve 1 = Theophylline 1 mg/ml (6 animals, 13 processes). Curve 2 = BAL 4×10^{-4} M (3 animals, 5 processes). Curve 3 = Mersalyl 4×10^{-4} M plus BAL 4×10^{-4} (4 animals, 11 processes). Mean selected standard curve and minimum slope line as in fig. 1.

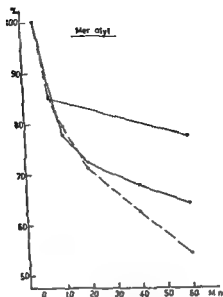


Fig 3

Mercuryl 2×1 ml injected intramuscularly *in vivo* Coordinates as in fig 1 Discontinuous curve (6 animals 16 processes) Continuous curve = mean standard curve with buffer solution, pH 7.4 Minimum slope line from 85 per cent at 5 minutes to mean value plus three standard deviations at 60 minutes

Since in these experiments the drug is added before the *in vitro* experiment a slightly different standard curve is used (4)

Discussion

The formal nature of the mechanism of organic mercurials on transport is complex and not yet wholly elucidated. The action of mercurials in the kidney might partly be explained by changes in permeability of cellular membranes but primarily it involves an attachment of mercury to a sulphydryl group of an enzyme that helps to generate energy for sodium transport or to a sodium carrier.

Swelling of rat kidney slices have been observed after treatment with orga

nic mercurials (16 19) It was suggested that this effect was due to an increased cell permeability rather than to an effect on active transport

Bivalent mercury has a great affinity for sulfhydryl groups of protein molecules It has been assumed that the mercuric ion of organomercurial diuretics inhibits the enzymes involved in sodium transport by forming a mercaptide complex with the enzyme protein Mercury which reacts with sulfhydryl groups of tissues may be removed from the receptor sites by the sulfhydryl compound dimercaprol, BAL A reduction of proteinbound sulfhydryl groups is correlated with the occurrence of diuresis The diuretic effect of mercurials is apparently not due to inhibition of succinic dehydrogenase since therapeutic doses of mersalyl fail to inhibit oxidative enzymes of the Krebs cycle Inhibition of succinate dehydrogenase in the kidney tubules with organic mercurials occurs only after heavy doses

It can be noted however that in the ciliary processes in the eye there is histochemical evidence for succinic dehydrogenase (2 10 12) Furthermore, Cole (13) could establish in *in vitro* experiments that succinate and citrate increased the transepithelial potential and the short circuit current of the ciliary processes Cole suggested that the active sodium transport from stroma to aqueous is driven from the citric acid cycle oxidation

A considerable body of experimental evidence now suggests that the Na⁺ K⁺ dependent ATPase activity found in different epithelial cell membranes (1 19 21) including the ciliary processes of the eye (6 20) is a property of the coupled transport for sodium and potassium in the membrane Recently Jones et al (15) established that organic mercurials *in vitro* and *in vivo* inhibited Na⁺ K⁺ dependent ATPase activity in membrane fragments from kidneys of rats It was suggested that the mercurials act by directly attacking sodium and potassium binding sites of the transport system (see also review by Cafruny (9) 1968)

As well as in the kidney mersalyl inhibits active transport in other epithelial systems as for instance in the frog skin Using about the same concentration as in our experiments Linderholm (17) found that mersalyl (10^{-4} M) inhibited active transport of sodium across the frog skin *in vitro*

With the present *in vitro* technique the influence on transport by various drugs can be studied The direction of the transport is more difficult to analyze The net result of a less than normal shrinkage of the ciliary processes would indicate an inhibited secretion of aqueous This effect could be due to a decreased transport "inwards" to the aqueous side or to a stimulated transport "outwards" to the ciliary stroma A toxic effect leading to a complete stoppage of transport by cell death would with similar outer and inner environment of the processes be expected to lead to a preservation of the zero time value of the area of the ciliary processes An enlargement instead of a shrinkage of the processes (i.e. a swelling of the stroma) would indicate a stimulated transport "outwards" to the ciliary stroma with accompanying water It is then

assumed that the technique is an indicator of a transport across the membrane system (*i.e.* from outside to inside). The photographic recordings which in previous experiments (3,4,5) showed a uniform decrease in area with time lent support to this view.

An enlargement of the ciliary processes as was found in the present experiments is compatible with a swelling of the stroma but on the other hand a swelling in the epithelial cells cannot be ruled out. It is not possible from the present data to decide conclusively between these alternatives. A suggestion that a stromal process is here also involved is the fact that the pictures from experiments with strong *mersalyl* concentrations showed ciliary processes which increased uniformly exactly as in previous experiments there was a uniform decrease. It would be difficult to understand that if there had been a swelling in the epithelial cells this would occur to the same extent over the whole area resulting in a uniform increase. An irregular increase of the ciliary processes would seem more likely if the swelling had occurred in the epithelial cells.

With the technique used mercury is as yet the only drug found to have caused an enlargement instead of a shrinkage of the ciliary processes. Pilocarpine, epinephrine, acetazolamide and metabolic inhibitors as for instance ouabain all gave a less than normal shrinkage (3,4,5).

If organic mercury should exert a similar action in the ciliary processes as in other epithelial transport systems the observed enlargement of the ciliary processes after mercurial treatment might be compatible with different possibilities.

An increased membrane permeability might be expected to lead to a swelling in the epithelial cells but in the absence of an osmotic gradient it would not lead to a swelling of the stroma. An inhibition of the sodium pump in the ciliary epithelial membrane system would cause a swelling in the epithelial cells. An effect on coupled opposing systems of transport of ions and water across the ciliary epithelial cell layers would hypothetically result in a swelling of the stroma. These transport systems are then assumed to work with some kind of feedback system in such a manner that an inhibition of for instance a transport system inwards (*i.e.* the sodium pump) would lead to the stimulation of another process of transport of ions and water in the opposite direction.

The negative results on the secretory activity in the eye from animals injected with *mersalyl* *in vivo* were not unexpected. The organic mercurials have been shown to have a selective affinity to the kidney (8) and such diuretics did not produce a fall in intraocular pressure in human subjects (11). The reported transitory decrease in IOP in normal and nephrectomised rabbits from intramuscular injections of organic mercurials *in vivo* (1) can hardly be taken as evidence for a block of the sodium pump in the ciliary epithelium. The authors were also unable to demonstrate any effect from subconjunctival or topical administration.

Summary

Mersalyl in a concentration from 0.1 mg/ml in the bathing medium caused an enlargement of the rabbit ciliary processes *in vitro*. Theophylline was without effect. Dimercaprol BAL which in itself was without effect on the secretory pumping of the ciliary processes abolished in equimolar concentration the mersalyl effect. *In vivo* injections of mersalyl were without effect. Influence on secretion *in vitro* and particularly across the ciliary epithelial cell membranes is difficult to interpret in terms of directions of transport. The action of mersalyl on the ciliary processes *in vitro* is discussed in relation to its presupposed action on other epithelial active transport systems. It is suggested that the marked effect of mersalyl causing an enlargement instead of the normal shrinkage of the ciliary processes with time might be due to interference with active cation transport possibly by its action on Na⁺K⁺ dependent ATPase or on enzymes of the citric acid cycle. Blocking of transport to the aqueous side or stimulation of transport to the stroma are both potential possibilities.

References

- 1 Auricchio G, Diotallevi M. Azione dei diuretici mercuriali sul tono oculare. *Ann. di Ottal. e clin. Oculist.* 89, 163, 1963.
- 2 Berggren L. A histochemical study of the anterior segment of the eye in gold id. (Idus Idus L.) chicken, rabbit and man with special regard to the angle of the anterior chamber. *Acta Soc. Med. Ups.* 62, 157, 1957.
- 3 Berggren L. Direct observation of secretory pumping *in vitro* of the rabbit eye ciliary processes. Influence of ion milieu and carbonic anhydrase inhibition. *Invest. Ophthalmol.* 3, 266, 1964.
- 4 Berggren L. Effect of composition of medium and of metabolic inhibitors on secretion *in vitro* by the ciliary processes of the rabbit eye. *Invest. Ophthalmol.* 4, 3, 1965.
- 5 Berggren L. Effect of parasympathomimetic and sympathomimetic drugs on secretion *in vitro* by the ciliary processes of the rabbit eye. *Invest. Ophthalmol.* 4, 91, 1965.
- 6 Bonting S L, Simon K A, & Hawkins N M. Studies on sodium potassium activated adenosine triphosphatase I. *Arch. Biochem. Biophys.* 95, 416, 1961.
- 7 Bonting S L, Caravaggio L L, & Hawkins N M. Studies on sodium potassium activated adenosinetriphosphatase IV. *Arch. Biochem. Biophys.* 98, 415, 1963.
- 8 Burghraef R R M & Pitts R F. The distribution of chlormerodrin (Neohydrin) in tissues of the rat and dog. *J. clin. Invest.* 35, 31, 1956.
- 9 Cafruny F J. The site and mechanism of action of mercurial diuretics. *Pharmacol. Rev.* 20, 59, 1968.
- 10 Cameron E & Cole D F. Succinic dehydrogenase in rabbit ciliary epithelium. *Exp. Eye Res.* 2, 25, 1963.
- 11 Campbell D A. Diuretics and the eye. *Brit. Med. J.* 2, 46, 1961.

- 12 Cole D F. Utilization of carbohydrate metabolites in the rabbit ciliary epithelium. *Exp Eye Res.* 9 284 1963
- 13 Cole D F. Citrate cycle and active sodium transport in rabbit ciliary epithelium. *Exp Eye Res* 4 211 1965
- 14 Holm Jensen I. Osmotic regulation in *Daphnia magna* under physiological conditions and in the presence of heavy metals. *Kgl Danske Vidensk Selsk. Biol Medd* 40 1 1948
- 15 Jones V D, Lockett G & Landon E J. A cellular action of mercurial diuretics. *J Pharmacol and Exp Ther* 147 23 1965
- 16 Kleineller A & Cort J H. The mechanism of action of mercurial preparations on transport processes and the role of thiol groups in the cell membrane of renal tubular cells. *Biochem J* 67 15 1957
- 17 Linderholm H. Active transport of ions through frog skin with special reference to the action of certain diuretics. *Acta physiol Scand. suppl* 97 1952
- 18 Post R L, Merritt C R, Kinsolving R C & Albright C D. Membrane adenosine triphosphatase as a participant in the active transport of sodium and potassium in the human erythrocyte. *J Biol Chem* 235 1496 1960
- 19 Robinson J R. The effect of sodium and chloride ions upon swelling of rat kidney slices treated with a mercurial diuretic. *J Physiol* 134 216 1956
- 20 Simon A A, Benning S L & Hawkins N M. Studies on sodium potassium activated adenosine triphosphatase II. *Exp Eye Res* 1 255 1962
- 21 Skou J C. The influence of some cations on an adenosine triphosphatase from peripheral nerves. *Biochim Biophys Acta* 43 394 1957

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SECRETORY ACTIVITY IN VITRO OF THE RABBIT EYE CILIARY PROCESSES INCUBATED WITH CORTICOSTEROIDS NEUROHYPOPHYSEAL HORMONES AND ASCORBIC ACID

BY

LENNART BERGGREN

Corticosteroids have pronounced effects on the exchange of sodium and potassium but a full analysis of their effects on transport mechanisms and directions of transport is still lacking. The mineral corticoids stimulate the sodium hydrogen (or potassium) exchange in the distal tubules and they decrease the sodium content and increase the potassium content in for instance sweat and saliva. In the eye corticosteroids have well established pressure increasing effects on intraocular pressure. Here also their basic action is unsolved although the pressure increasing effects are mostly attributed to effects on outflow facility. Possible effects on secretion however have never been ruled out. Linner (1969) has presented evidence that prednisolone caused an elevation of the intraocular pressure with no change in the facility of outflow or in the episcleral venous pressure. The effect was explained to be caused by an increase in the rate of aqueous flow. It can be noted that Jackson & Waitzman (20) reported a dual intraocular pressure response and the secondary hypertensive response was accompanied by changes in flow. They could also demonstrate a sustained hypotension by aldosterone probably caused by decreased aqueous flow.

However aldosterone has a stimulatory effect on sodium transport in *in vitro* experiments on toad bladder (12) and Cole (10) showed that the aldosterone antagonist spiro lactone reduced sodium and water influx across the ciliary epithelium in the rabbit eye.

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The vasopressor hormone of the posterior pituitary lobe has well known effects on the resorption of water by its action on the renal tubules Becker et al (3 11) have tested vasopressin on human and rabbit eyes Vasopressin lowered the intraocular pressure when applied locally and tonography revealed that the intraocular pressure drop was due to suppression of aqueous flow

Neurohypophyseal hormones increase *in vitro* the rate of water uptake and the rate of active sodium transport across the frog skin (15) and the toad bladder (14) presumably by increasing the pore size of some layer in the skin

Ascorbic acid is secreted into the aqueous humor in excessive amounts but its action on the inflow and/or outflow is not clearly understood A review of the possible functions of ascorbic acid in the eye is given by Heath (18) In normal human subjects Linner (24 25) could show that oral and topical administration of ascorbic acid gave a small but significant decrease of the intraocular pressure Oral dosages of 0.5-1.0 g/day or application of a 10 per cent eye drop solution three times a day were given in order to influence the intraocular pressure The experimental results were in favour of a reduction in the rate of flow The findings have been confirmed (?) but failures to decrease IOP with ascorbic acid are also reported (13 14)

In the present paper the previously described method of studying secretory activity of the ciliary processes *in vitro* was used (6 7) in order to determine if corticosteroids neurohypophyseal hormones or ascorbic acid could influence this type of secretory activity

Material and Methods

Male albino rabbits weighing about 2 kg and fed a diet of hay and oats and water ad lib were used

In vitro technique Secretory pumping has been described in detail previously (6 7) The gradual shrinkage in size that the ciliary processes show on incubation in a physiologic buffer solution was taken as a measure of secretory activity The tissue fluid of the ciliary processes was replaced with a physiological buffer solution by perfusion through a carotid artery in the living animal Sections of iris ciliary body were prepared and put into a bath containing the same buffer solution Care was taken to prevent secretion as much as possible up to the incubation *in vitro* The area of a transverse optical section of the processes was photographed intermittently for one hour and one to four processes were generally suitable for planimetry The reduction in area of the different processes was calculated in per cent from the zero time value and averaged for each time The single eye was treated as the statistical unit Ciliary processes showing a shrinkage of 1 per cent or less at 5 minutes were considered to have impaired function Those with a shrinkage of 15 per cent or more at 5 minutes

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However aldosterone has a stimulatory effect on sodium transport in *in vitro* experiments on toad bladder (12) and Cole (10) showed that the aldosterone antagonist spiro lactone reduced sodium and water influx across the ciliary epithelium in the rabbit eye.

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Table 1

Shrinkage of ciliary processes *in vitro* after incubation with various drugs Effect 0 = normal shrinkage Buffer solution pH 7.4 unless otherwise indicated

Drug	Number of expts animals/processes	Final conc/ml in medium	Effect
Hydrocortisone	4/9	1 mg	0
Prednisolone	4/8	0.5 mg	0
Dexamethasone	4/11	0.05 mg	0
Dexamethasone 1 m ¹⁾	7/21		0
Aldosterone	4/11	0.01 mg	0
Corticotropin	6/12	0.01 IU	0
Corticotropin 1 m ²⁾	6/17		0
Vasopressin	4/10	0.2 IU	0
Oxytocin	5/14	0.1 IU	0
Ascorbic acid	3/16	20 µg	0
Ascorbic acid	3/12	100 µg	0
Ascorbic acid ³⁾	5/20	100 µg	0
Ascorbic acid	2/8	200 µg	0
Ascorbic acid	8/15	1 mg	0
Ascorbic acid ⁴⁾	6/13	1 mg	0
Ascorbic acid pH 7.0 ⁴⁾	5/13	1 mg	0

1) 4 mg dexamethasone 1 m during 3 days before *in vitro* experiment

2) 15 IU corticotropin 6 and 3 days before *in vitro* experiment

3) Ascorbic acid added to the perfusion fluid as well as to the bathing solution in a concentration of 100 microg/ml

4) Ascorbic acid added to the bathing solution 6 times during the first half hour of the *in vitro* experiment

were below a line from 85 per cent at 5 minutes to the mean value plus 3 standard deviations at 60 minutes Table 1 and fig. 1

Ascorbic acid The effect of ascorbic acid was tested in various ways. The results are based from a total of 32 rabbits Table 1

With the common *in vitro* technique ascorbic acid was put into the bath at plus 7 minutes. A concentration from 20 microg/ml to 1 mg/ml final concentration in the bathing medium was without effect on the normal shrinkage of the ciliary processes.

The effect of ascorbic acid was also tested with ascorbic acid in a concentration of 100 microg/ml in the perfusion fluid as well as in the bathing medium and a pH 4. These results also were negative.

In order to eliminate a possible oxidation of ascorbic acid during the *in vitro*

were assumed to have too small a residual capacity. In control experiments the processes shrink down to about 65 per cent of the zero time value in one hour. The minimum slope line is defined as a straight line from the point of 85 per cent remaining surface area at 5 minutes from zero time to the mean value plus 3 standard deviations at 60 minutes. Blocking effects on secretion were considered to have occurred if the mean curves of shrinkage after the addition of drugs (always at plus 5 min) were above the minimum slope line. This criterion allows relatively small samples to be used. Detail variations of the technique is reported under Results.

Drugs

Buffer solution The physiological buffer solution was made up as described previously (7) and prepared from chemicals of analytical grade. With the concentrations expressed in mM/L the composition was NaCl 150 KCl 3 Mg SO_4 1 H₂O 1 glucose 7. The solution was tris buffered and equilibrated with 95 per cent O₂/5 per cent CO₂ to a pH of 7.4 or in some experiments 7.0.

Hydrocortisone Solu Cortef® hydrocortisone sodium succinate 50 mg/ml Ampoules of 2 ml (Upjohn Co Mich USA)

Prednisolone Precortalon aquosum® prednisolone sodium succinate 25 mg/ml Ampoules of 1 ml (Organon Holland)

Dexamethasone Decadron® fluor methyl prednisolone 4 mg/ml Ampoules of 1 ml (MSD USA)

Aldosterone Aldocorten® 0.5 mg/ml Ampoules of 1 ml (Ciba Switzerland)

Corticotropin Cortrophine® 10 IU/ml Ampoules of 5 ml (Organon Holland)

Vasopressin Postacton® 20 IU/ml Ampoules of 1 ml (Ferring Sweden)

Oxytocin Partocon® 10 IU/ml Ampoules of 1 ml (Ferring Sweden)

Ascorbic acid 500 mg/ml Ampoules of 1 ml (ACO Sweden)

Results

Corticosteroids and neurohypophyseal hormones The results from 44 rabbit experiments are summarized in table I.

It was not possible to influence significantly the *in vitro* secretory activity by the administration in the bathing medium of the following drugs: Hydrocortisone, prednisolone, dexamethasone (fig 1), aldosterone, corticotropin, vasopressin and oxytocin. The effect of dexamethasone and corticotropin was also tested after intramuscular injection of these drugs. Dexamethasone (4 mg) was given during 3 days before the *in vitro* experiment. Corticotropin (15 IU) was given 6 and 3 days before the *in vitro* experiment. The *in vitro* secretory activity was then studied without addition of any drug in the bathing medium. The results from these experiments were also within normal limits.

The mean curves from all these experiments showed a gradual shrinkage of the ciliary processes which was within the defined normal range i.e. the curves

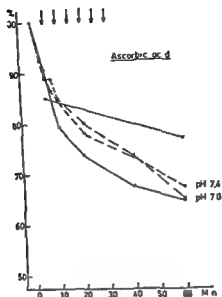


Fig 2

Ascorbic acid added to the bathing solution at arrows (final concentration in the bath 1 mg/ml). Coordinates as in fig 1. Mean selected time shrinkage curves. Curve pH 7.4 (4 animals, 13 processes). Curve pH 7.0 (5 animals, 13 processes). Continuous curve = mean selected standard curve and minimum slope line as in fig 1.

ciliary processes and ultimately on aqueous secretion. With regard to the effects on sodium and potassium transport in other epithelial systems by corticosteroids a similar effect in the ciliary processes would not have seemed unlikely. On the other hand the negative results cannot be taken as evidence that corticosteroids do not influence transport in the ciliary processes of the eye. It can be noted that corticosteroids have structural similarities to the cardiac aglucones like ouabain. This drug has repeatedly been shown to have a strong inhibitory effect on active sodium transport in many epithelial systems including the eye (4, 7, 9). The strong effect of ouabain and the weak effect of corticosteroids on cation transport over the erythrocyte membrane has led to the hypothesis advanced by Glynn (16) that corticosteroids in order to be effective have to be transformed to substances similar to the cardiac aglucones. Since a transformation of this kind is unlikely to occur *in vitro* possible effects will not easily be demonstrated.

The stimulating effect of the neurohypophyseal hormones and aldosterone on the transport of sodium ions across amphibian epithelial layers *in vitro* has been established for frog skin (13) as well as for toad bladder (12, 14). The results are in support of the idea of a permeability effect. Spirolactone, an aldo-

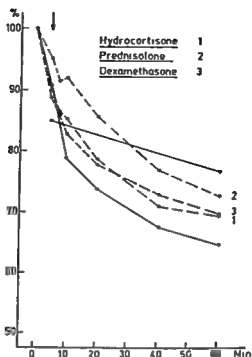


Fig 1

Hydrocortisone prednisolone and dexamethasone added to the bathing solution at arrow Ordinate = Calculation of transverse section area of ciliary processes in per cent Zero value = 100 per cent Abscissa = time in minutes Mean selected time shrinkage curves Curve 1 = Hydrocortisone succinate 1 mg/ml (4 animals 9 processes) Curve 2 = Prednisolone succinate 0.5 mg/ml (4 animals 8 processes) Curve 3 = Dexamethasone 0.05 mg/ml (4 animals 11 processes) Continuous curve = mean selected standard curve with buffer solution pH 7.4 Minimum slope line from 85 per cent at 5 minutes to mean standard value plus three standard deviations at 60 minutes

experiment the following change was made in the *in vitro* technique Of the total dose giving a final concentration of 1 mg/ml in the bath 50 per cent of the drug was given at plus 5 minutes and 10 per cent of the drug then every 5 minutes up to 30 minutes incubation time Two pH values pH 7.4 and pH 7.0 were tested with this technique Both series were within normal limits

Summing up ascorbic acid was without effect on the normal secretory activity *in vitro* of the ciliary processes of the rabbit eye at pH 7.4 and 7.0 and it was also ineffective if administered to the bathing medium intermittently during half an hour or if the bathing medium as well as the perfusion fluid contained ascorbic acid

Discussion

The present *in vitro* experiments could not establish any potential role of corticosteroids or of neurohypophyseal hormones on transport processes in the

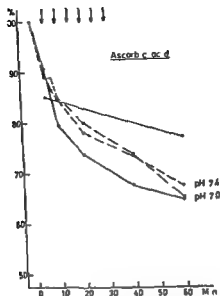


Fig 2

Ascorbic acid added to the bathing solution at arrows (final concentration in the bath 1 mg/ml) Coordinates as in fig 1 Mean selected time shrinkage curves Curve pH 7.4 (6 animals 12 processes) Curve pH 7.0 (5 animals 13 processes) Continuous curve = mean selected standard curve and minimum slope line as in fig 1

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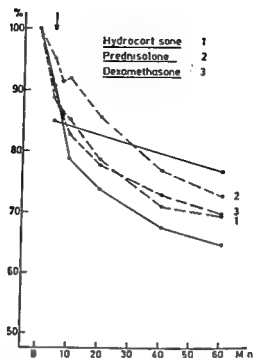


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sults are in support of the idea of a permeability effect Spirolactone an aldosterone *in vitro* secretion by ascorbic acid indirectly support this latter view

The same kind of reasoning could be adopted towards some effects of corticosteroids The absence of effect by corticosteroids on *in vitro* secretory pumping (in the present experiments) and on aqueous flow (1) (measured by fluorophotometry) favour a hypothesis that the pressure increase found by Linner (23) without change in C values (measured by tonography) or in F values (measured by the suction cup) might be due to an effect on routes of outflow via unconventional routes

Summary

The shrinkage of ciliary processes *in vitro* is taken as a measure of secretory activity It was not possible to influence the normal shrinkage with time with the following drugs and concentrations in the bathing medium Hydrocortisone 1 mg/ml prednisolone 0.5 mg/ml dexamethasone 0.05 mg/ml aldosterone 0.01 mg/ml corticotropine 0.01 IU/ml vasopressin 0.2 IU/ml oxytocin 0.1 IU/ml and ascorbic acid up to a concentration of 1 mg/ml

References

- 1 Anselmi P Bron A J & Maurice D M Action of drugs on the aqueous flow in man measured by fluorophotometry *Exp Eye Res* 1 487 1963
- 2 Armaty M In *Drug mechanisms in glaucoma* The Gilston Glaucoma Symp 1964 p 163 Churchill Ltd London 1966
- 3 Becker B & Christensen H E Beta hypophamine (Vasopressin) Its effect upon intraocular pressure and aqueous flow in normal and glaucomatous eyes *Arch Ophthalmol* 56 1 1956
- 4 Becker H Ouabain and aqueous humor dynamics in the rabbit eye *Invest Ophthalmol* 2 325 1963
- 5 Becker H Ascorbate transport in guinea pig eyes *Invest Ophthalmol* 6 410 1967
- 6 Berggren L Direct observation of secretory pumping *in vitro* of the rabbit eye ciliary processes Influence of milieu and carbonic anhydrase inhibition. *Invest Ophthalmol* 3 266 1964
- 7 Berggren L Effect of composition and of metabolic inhibitors on secretion *in vitro* by the ciliary processes of the rabbit eye *Invest Ophthalmol* 4 83 1965
- 8 Bill A The aqueous humor drainage mechanism in the cynomolgus monkey (*Macaca mullis*) with evidence for unconventional routes *Invest Ophthalmol* 4 911 1965
- 9 Cle D F Effects of some metabolic inhibitors upon the formation of the aqueous humor in rabbits *Brit J Ophthalmol* 44 139 1960
- 10 Cle D F Reduction in aqueous humor formation as caused by iodate spirolactone and polyphloretin phosphate *Brit J Ophthalmol* 46 791 1967

sterone antagonist reduced sodium and water influx across the ciliary epithelium in the rabbit eye (10)

In the present *in vitro* experiments there was no effect from neurohypophyseal hormones or aldosterone. It should be noted however that the present *in vitro* technique is more appropriate to demonstrate inhibition than stimulation. A hypothetical stimulation would give rise to an increased rate of shrinkage or a more pronounced total shrinkage at the end of the experiment. This would be difficult to show since the normal shrinkage curve has already a rather steep slope and the 60 minutes value is probably a lower limit value. Further incubation does not cause a further shrinkage of the ciliary processes.

The excess of ascorbic acid in the aqueous and its selective transport mechanism has for a long time been a subject of considerable research work but there is still surprisingly little knowledge of its basic role in the eye (see reviews by Kinsey (21) and Linnér (26)). Among pertinent questions which still remain to be answered are: a) how ascorbic acid itself is transported into the aqueous; b) whether ascorbic acid might be a necessary component in other active transport processes across the ciliary epithelial layers; c) or whether the excess of ascorbic acid in the aqueous might play a role in metabolic processes in the anterior parts of the eye for instance on the outflow resistance in the trabecular meshwork.

Ascorbic acid is transported into the retina as well as into the aqueous via the ciliary processes. In the retina the transport is linked with the movement of sodium and the transport is inhibited by ouabain and DNP (19). In the ciliary processes the active sodium transport and the secretory pumping with our technique show similar characteristics (see review by Linner (26)). Furthermore Becker (5) has demonstrated that the accumulation of ascorbic acid in ciliary body preparations from guinea pigs was inhibited by ouabain and DNP. The accumulation was also dependent on the presence of Na and K. These findings suggested that the ascorbic acid transport in the ciliary processes was closely related to Na K dependent ATPase activity.

The findings by Linner (24-25) that ascorbic acid *in vivo* could produce a fall in IOP gave rise to the present *in vitro* experiments. However with our technique an excess of ascorbic acid did not influence the normal secretory activity in the ciliary processes. Unfortunately there is no way of demonstrating the possible effects of the reversed condition i.e. a total lack of ascorbic acid. Even animals on the point of death from scurvy (scurbutic guinea pigs) have apparently sufficient content of ascorbic acid in the aqueous (27).

Since the pressure drop by ascorbic acid in Linnér's (24-25) *in vivo* experiments occurred without change in C values it seemed likely that it was caused by a decrease in flow. However Linner also discussed the hypothetical possibility that in his experiments an effect on outflow via unconventional uveoscleral routes as described by Bill (8) might be involved. Our negative results

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FURTHER STUDIES ON THE EFFECT OF AUTONOMOUS DRUGS ON IN VITRO SECRETORY ACTIVITY OF THE RABBIT EYE CILIARY PROCESSES

- A Inhibition of the pilocarpine effect by isopilocarpine
arecoline and atropine
B Influence of isoproterenol and norepinephrine

BY

LENNART BERGGREN

The blocking effect of pilocarpine on the secretory pumping *in vitro* of the rabbit eye ciliary processes has been established repeatedly (5,6). In the present experiments the pilocarpine concentration in the bathing medium was 10^{-6} M final concentration which was regarded as giving a reliable blocking effect.

Another parasympathomimetic alkaloid arecoline had no significant effect up to a concentration of 10^{-4} M in previous experiments (5). The parasympatholytic agent atropine inhibited secretory activity *in vitro* only in a concentration of 10^{-4} M but not at 10^{-6} M (5).

The experimental set up does not allow different drugs to be added successively to the medium in the same experiment. The period for studying drug effects is restricted to between 5-60 minutes. A time of up to 5 min is needed to check that the surviving ciliary processes are in normal condition and after one hour the ciliary processes have pumped themselves dry and might be regarded as less viable. Thus in order to study drug interaction each drug must be tested separately as well as simultaneously.

The demonstrated inhibitory effect of epinephrine on the normal shrinkage

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- 11 Constant M J & Becker B Experimental tonography II The effects of vasopressin chlorpromazine and phentolamine methanesulfonate. Arch Ophthalmol 56 19 1956
- 12 Dalton T & Smart R S Effect of hormones on the permeability of toad bladder (*Bufo marinus*) Biochim Biophys Acta 135 1059 1967
- 13 Esila R Liesmaa M Tenhunen T & Tuovinen E The effect of ascorbic acid on the intraocular pressure and the aqueous humor of the rabbit eye Acta Ophthalmol 44 631 1966
- 14 Frazer H S Dempsey E H & Leaf A Movement of sodium across the mucosal surface of the isolated toad bladder and its modification by vasopressin J gen Physiol 45 529 1962
- 15 Fuhrman F A & Ussing H H A characteristic response of the isolated frog skin potential to neurohypophyseal principles and its relation to the transport of sodium and water J cell comp Physiol 39 109 1951
- 16 Glynn I M The action of cardiac glycosides on sodium and potassium movements in human red cells J Physiol 136 143 1957
- 17 Gnadinger M & Willome J Zur Frage der Wirkung von Ascorbinsäure auf den normalen intraocularen Druck bei lokaler Anwendung Klin Mbl Augenheilk 153 352 1963
- 18 Heath H The distribution and possible functions of ascorbic acid in the eye Exp Eye Res 1 362 1962
- 19 Heath H & Fiddick R The active transport of ascorbic acid by the rat retina. Exp Eye Res 5 156 1966
- 20 Jackson R T & Waitman M B Effects of some steroids on aqueous humor dynamics Exp Eye Res 4 112 1965
- 21 Kinsey V E Chemistry and dynamics of aqueous humor in *The Rabbit in Eye Research* ed Jack H Prince Charles C Thomas Publ Springfield Ill USA 1964
- 22 Linner E The effect of prednisolone on aqueous humor dynamics Acta Soc Med Ups 62 186 1959
- 23 Linner E Adrenocortical steroids and aqueous humour dynamics Documenta Ophthalmologica 13 210 1959
- 24 Linner E Intraocular pressure regulation and ascorbic acid Acta Soc Med Ups 69 225 1964
- 25 Linner E The effect of ascorbic acid on intraocular pressure In *Drug mechanisms in glaucoma* The Gilston Glaucoma Symp 1964 p 153 Churchill Ltd London 1966
- 26 Linner E Biochemical basis of aqueous secretion In *Biochemistry of the Eye* Symp Tutzing Castle 1966 p 156 Karger Basel New York 1968
- 27 Sabatini P L Rosen H Geever E F & Leenson S M Scurvy, ascorbic acid concentration and collagen formation in the guinea pig eye Arch Ophthalmol 63 32 1961

The solution was tris buffered and equilibrated with 95 per cent O_2 5 per cent CO_2 in a pH of 7.4 or in some experiments 7.0

Pilocarpine Mol w 208 The hydrochloride was used

Atropine Mol w 269 The sulfate was used

Isopilocarpine Mol w 208 The stereoisomer of pilocarpine The hydrochloride was used The supply of isopilocarpine was a generous gift from Dr H W Voigtlander E. Merck AG Darmstadt Germany

Arecoline Mol w 155 The hydrobromide was used

Isoproterenol Mol w 211 Isopropylidene isoproterenol sulfate (Abbot Lab Chicago Ill US A) 10 per cent dry powder ampoule

Norepinephrine Mol w 169 Nor Exadria Conc® norepinephrine 1 base (Astra Sodertälje Sweden) Ampoules of 2 ml containing 1 mg norepinephrine base/ml

Results

Pilocarpine in a final concentration of 10^{-5} M once more had a blocking effect on the shrinkage of the ciliary processes *in vitro* (5 animals 19 processes) (Fig 1)

Atropine in a final concentration of 10^{-7} M was without effect (6 animals 17 processes) (Fig 1) In previous experiments (5) a possible inhibition at 10^{-7} M was noted Rabbits are in general rather insensitive to atropine compared to humans and monkeys but the sensitivity can differ in different strains of rabbits

A combination of pilocarpine 10^{-5} M and atropine 10^{-7} M was without effect on the normal shrinkage of the ciliary processes (6 animals 17 processes) In fact the pilocarpine atropine curve was very similar to the normal curve (Fig 1)

Pilocarpine atropine experiments were also done with a more uniform animal group in the following manner The *in vitro* experiments were repeated with one pilocarpine experiment one atropine experiment and one pilocarpine atropine experiment each day for three days and in a variable order The experiments on the same day were performed on animals from the same stock The results above were confirmed Pilocarpine 10^{-5} M (3 animals 11 processes) gave an inhibition Atropine 10^{-7} M (3 animals 10 processes) gave no inhibition The combination pilocarpine 10^{-5} M and atropine 10^{-7} M (3 animals 7 processes) gave no inhibition (Fig 2) These experiments showed that it is possible to abolish the pilocarpine effect on secretion *in vitro* by atropine

The stereoisomer of pilocarpine isopilocarpine gave a gradual inhibition of the shrinkage of the ciliary processes but even at a final concentration of 10^{-4} M it did not fulfill the given criteria for a blocking effect on secretion (Fig 3) It was thus not possible to reproduce the pilocarpine effect using its stereoisomer isopilocarpine Furthermore a combination of isopilocarpine

of the ciliary processes (5) made it of interest to test also other adrenergics such as the alpha adrenergic norepinephrine and the beta adrenergic isoproterenol

Material and Methods

Male albino rabbits weighing about 2 kg and fed a diet of hay and oats and water ad lib were used

In vitro technique Secretory pumping has been described in detail previously (3,4). The gradual shrinkage in size that the ciliary processes show on incubation in a physiological buffer solution was taken as a measure of secretory activity. The tissue fluid of the ciliary processes was replaced with a physiological buffer solution by perfusion through a carotid artery in the living animal. Sections of iris ciliary body were prepared and put into a bath containing the same buffer solution. Care was taken to prevent secretion as much as possible up to the incubation *in vitro*. The area of a transverse optical section of the processes was photographed intermittently for one hour and one to four processes were generally suitable for planimetry. The reduction in area of the different processes was calculated in per cent from the zero time value and averaged for each time. The single eye was treated as the statistical unit. Ciliary processes showing a shrinkage of 1 per cent or less at 5 minutes were considered to have impaired function. Those with a shrinkage of 15 per cent or more at 5 minutes were assumed to have too small a residual capacity. In control experiments the processes shrink down to about 65 per cent of the zero time value in one hour. The minimum slope line is defined as a straight line from the point of 85 per cent remaining surface area at 5 minutes from zero time to the mean value plus 3 standard deviations at 60 minutes. Blocking effects on secretion were considered to have occurred if the mean curves of shrinkage after the addition of drugs (always at plus 5 min) were above the minimum slope line. This criterion allows relatively small samples to be used.

In vivo In some experiments drugs were injected *in vivo* prior to the perfusion. In these experiments the *in vitro* incubation was done with buffer solution only and without the addition of test drugs. A slightly different standard curve is then used as described previously (4).

Drugs

Buffer solution The physiological buffer solution was made up as described previously (4) and prepared from chemicals of analytical grade. With the concentrations expressed in mM/L the composition was NaCl 150 KCl 3 MgSO₄ 7 H₂O 1 glucose 7

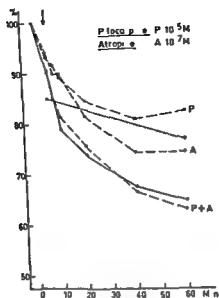


Fig 9

Pilocarpine atropine and pilocarpine plus atropine added to the bathing solution at arrow Coordinates as in fig 1 Mean selected time shrinkage curves Animals from the same stock and one experiment of each kind on the same day Curve P = pilocarpine 10^{-4} M (3 animals 11 processes) Curve A = atropine 10^{-7} M (3 animals 10 processes) Curve P + A = pilocarpine 10^{-4} M plus atropine 10^{-7} M (3 animals 7 processes) Continuous curve = mean selected standard curve and minimum slope line as in fig 1

perfusion was without effect on the normal shrinkage of the ciliary processes (Fig 6) Pilocarpine but not isopilocarpine caused immediately a profuse salivation

Isoproterenol sulfate in a final concentration of 0.2 mg/ml in the bathing medium (6×10^{-4} M) did not affect the normal shrinkage of the ciliary processes at a pH of 7.0 (6 animals 15 processes) (Fig 7)

Norepinephrine up to a final concentration of 0.01 mg/ml in the bathing medium (6×10^{-5} M) did not affect the normal shrinkage of the ciliary processes at a pH of 7.0 (6 animals 12 processes) (Fig 7)

Discussion

In previous experiments pilocarpine caused a less than normal gradual shrinkage of the ciliary processes *in vitro* (> 6) The findings were interpreted as an

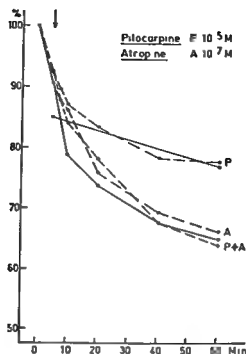


Fig 1

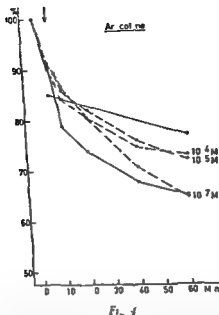
Pilocarpine atropine and pilocarpine plus atropine added to the bathing solution at arrow Ordinate = calculation of transverse section area of ciliary processes in per cent Zero value = 100 per cent Abscissa = time in minutes Mean selected time shrinkage curves Curve P = pilocarpine 10^{-5} M (5 animals 19 processes) Curve A = atropine 10^{-7} M (6 animals 17 processes) Curve P + A = pilocarpine 10^{-5} M plus atropine 10^{-7} M (6 animals 17 processes) Continuous curve = mean selected standard curve with buffer solution pH 7.4 Minimum slope line from 85 per cent at 5 minutes to mean standard value plus three standard deviations at 60 minutes

10^{-5} M and pilocarpine 10^{-5} M was without effect on the normal shrinkage of the ciliary processes (Fig 5)

Experiments with arecoline in a final concentration of 10^{-7} M to 10^{-4} M in the bathing medium suggest an effect but even the results from 10^{-4} M experiments were within normal limits (Fig 4) This confirms previous data (3) The pilocarpine effect was abolished by a combination of arecoline 10^{-5} M and pilocarpine 10^{-5} M (5 animals 23 processes fig 5) as well as by arecoline 10^{-7} M and pilocarpine 10^{-5} M (6 animals 14 processes)

A combination of the ineffective concentrations of isopilocarpine 10^{-5} M and arecoline 10^{-5} M (7 animals 24 processes fig 4) and isopilocarpine 10^{-5} M and arecoline 10^{-7} M (7 animals 20 processes) was also without effect on the normal shrinkage of the ciliary processes

Intravenous *in vivo* injections of pilocarpine (11 animals 43 processes) or isopilocarpine (3 animals 15 processes) 2 mg/kg body weight 5 minutes before



Arecoline added to the bathing solution at arrow. Coordinates as in fig. 1. Mean selected time shrinkage curves. Arecoline 10^{-4} M (6 animals, 13 processes). Arecoline 10^{-5} M (6 animals, 14 processes). Arecoline 10^{-7} M (6 animals, 12 processes). Continuous curve = mean selected standard curve and minimum slope line as in fig. 1.

have something to do with binding to cholinergic receptor sites. The parasympathomimetic drug arecoline could also block the pilocarpine effect. However, the weak effect or absence of effect on this type of secretory activity caused by other parasympathomimetics such as acetylcholine, carbacholine, and arecoline seems to be at variance with a view of truly cholinergic receptor sites.

Summing up, it has been established that in order to produce an effect on the *in vivo* shrinkage of the ciliary processes, both ends of the pilocarpine molecule seem to be of importance as well as their stereochemical position. With regard to the effect of pilocarpine on other epithelial transport systems *in vivo* and *in vitro* as well as its effect on accumulation *in vitro* by the ciliary processes of the eye, the results from pilocarpine experiments with the present *in vitro* technique seem to be more in favour of a stimulated transport outwards to the stroma than of an inhibited transport inwards to the aqueous.

The previously shown inhibitory effect of epinephrine (3) on the normal shrinkage of the ciliary processes was extremely difficult to establish. Many preparations had to be discarded due to the anatomical disarrangement of the ciliary processes caused by the addition of epinephrine. Using a rather high

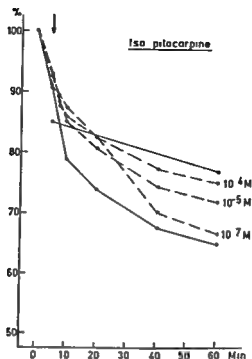


Fig 3

Isopilocarpine added to the bathing solution at arrow. Coordinates as in fig 1. Mean selected time shrinkage curves. Isopilocarpine 10^{-4} M (4 animals, 13 processes). Isopilocarpine 10^{-5} M (6 animals, 18 processes). Isopilocarpine 10^{-7} M (4 animals, 10 processes). Continuous curve = mean selected standard curve and minimum slope line as in fig 1.

inhibition of secretory activity. This inhibition might be due to an inhibited transport "inwards" to the aqueous or to a stimulated transport "outwards" to the stroma.

In other secretory systems as for instance saliva or sweat or tear production pilocarpine has a stimulatory effect. In *in vitro* transport experiments across the frog skin pilocarpine caused when applied to the outside a stimulatory effect on active sodium transport (8). In accumulation studies on rabbit eye ciliary processes it was shown that pilocarpine in low concentration stimulated the uptake of iodopyracet Diodrast (9) an anion which like iodide is known to be transported out of the eye *in vitro* as well as *in vivo* (1, 2, 7).

The pilocarpine effect with the present *in vitro* technique clearly shows that the stereochemical molecular configuration of pilocarpine is of importance. It has been demonstrated that the analogues of pilocarpine, i.e. pilocarpidine and pilosine were without effect (6) as well as now also the stereoisomer isopilocarpine. Furthermore the pilocarpine effect could be blocked by the parasympatholytic drug atropine which would suggest that the pilocarpine effect might

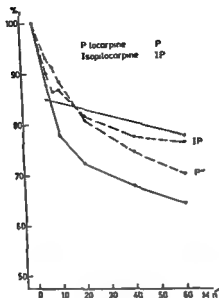


Fig 6

The animals injected intravenously in 1:10 with 2 mg/kg body weight of pilocarpine or isopilocarpine 5 minutes before perfusion. Coordinates as in fig 1. Mean time shrinkage curves. Curve P = pilocarpine (11 animals 43 processes). Curve IP = isopilocarpine (8 animals 13 processes). Continuous curve = mean standard curve with buffer solution, pH 7.4. Minimum slope line from 85 per cent at 5 minutes to mean standard value plus three standard deviations at 60 minutes.

isopilocarpine (10^{-6} M) as well as by atropine (10^{-7} M) and arecoline (10^{-7} M). It is suggested that the effect of pilocarpine might be due to its attachment to specifically oriented receptor sites in the ciliary processes.

Isoproterenol (0.2 mg/ml) and norepinephrine (0.01 mg/ml) did not influence the normal shrinkage of the ciliary processes indicating that the epinephrine effect on the secretory activity might be a metabolic effect.

References

1. Becker B. The transport of organic anions by the rabbit eye. I. *In vitro* iodopyracet (Diodrast) accumulation by ciliary body iris preparations. *Am J Ophthalmol* 50: 862, 1960.
2. Becker B. Iodide transport by the rabbit eye. *Am J Physiol* 200: 804, 1961.

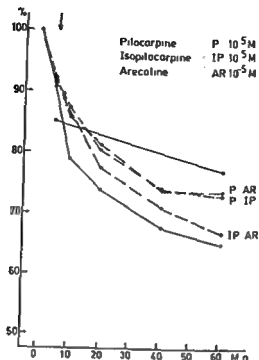


Fig 5

Combinations of pilocarpine isopilocarpine and arecoline added to the bathing solution at arrow Coordinates as in fig 1 Mean selected time shrinkage curves Curve P + AR = Pilocarpine 10^{-5} M plus arecoline 10^{-5} M (3 animals 23 processes) Curve P + IP = Pilocarpine 10^{-5} M plus isopilocarpine 10^{-5} M (6 animals 19 processes) Curve IP + AR = Isopilocarpine 10^{-5} M plus arecoline 10^{-5} M (7 animals 24 processes) Continuous curve = mean selected standard curve and minimum slope line as in fig 1

concentration 10^{-4} M and a pH of 7.0 some successful experiments showed a blocking effect Moreover this effect could be abolished by the adrenergic metabolic inhibitor BW 61 43 (N isopropyl methoxamine) In the present experiments the effect of epinephrine could not be reproduced either by the alpha adrenergic norepinephrine or by the beta adrenergic isoproterenol These findings might be interpreted as an indirect confirmation of the previously presented suggestion that the effect of epinephrine on *in vitro* secretory activity of the rabbit eye ciliary processes could be a metabolic effect

Summary

The inhibition of the normal shrinkage of the ciliary processes *in vitro* by pilocarpine (10^{-4} M) could be abolished by the stereoisomer of pilocarpine

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(Head Professor Salme Vannas M.D.)*

FLUORESCEIN ANGIOGRAPHY
OF THE OPTIC DISC AND THE PERIPAPILLARY AREA
IN CHRONIC GLAUCOMA

BY

CHRISTINA RAITTA and TIMO SARMELA

The optic disc receives its vasculature entirely from the ciliary system as was confirmed by Hayreh (1962) in an extensive investigation. In glaucomatous lesions of the optic disc a decreased vascularity of the disc might be expected. This was in fact the main finding in Hayreh's (1967) fluorescein study in glaucomatous patients.

The peripapillary region has special anatomic features as has been demonstrated by Michaelsson (1954) and by Allerman & Henkind (1968) for the retina. The choriocapillaris however is thought to be a continuous layer from the immediate peripapillary region to the ora serrata. This uniformity however has been a subject of debate. Hayreh & Perkins (1969) demonstrated experimentally diminished filling of the peripapillary choroidal vessels in acutely elevated I.O. pressure, a result that might point towards the possibility of different functional zones.

The present investigation was carried out in order to study the optic disc and peripapillary blood supply in chronic simple glaucoma and correlate the changes with visual field defects.

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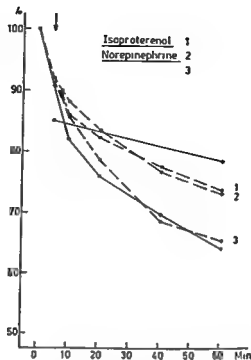


Fig 7

Isoproterenol and norepinephrine added to the bathing solution at arrow Coordinates as in fig 1 Mean selected time shrinkage curves Curve 1 = isoproterenol 0.9 mg/ml (6 animals 15 processes) Curve 2 = norepinephrine 10 microg/ml (6 animals 15 processes) Curve 3 = norepinephrine 0.1 microg/ml (6 animals 12 processes) Continuous curve = mean selected standard curve with buffer solution pH 7.0 Minimum slope line from 85 per cent at 5 minutes to mean standard value plus three standard deviations at 60 minutes

- 3 Berggren L Direct observation of secretory pumping *in vitro* of the rabbit eye ciliary processes Influence of ion milieu and carbonic anhydrase inhibition Invest Ophthal 3 266 1964
- 4 Berggren L Effect of composition of medium and of metabolic inhibitors on secretion *in vitro* by the ciliary processes of the rabbit eye Invest Ophthal 4 83 1965
- 5 Berggren L Effect of parasympathomimetic and sympathomimetic drugs on secretion *in vitro* by the ciliary processes of the rabbit eye Invest Ophthal 4 91 1965
- 6 Berggren L Comparison of ocular effects of pilocarpine pilocarpidine and pilosine Acta Ophthal 45 239 1967
- 7 Forbes M & Becker B The transport of organic anions by the rabbit eye II *In vivo* transport of iodopyracet (Diodrast) Am J Ophthal 50 867 1960
- 8 Kirshner L B The effect of atropine and the curares on the active transport of sodium by the skin of *Rana esculenta* J cell comp Physiol 45 89 1955
- 9 Walinder P E Influence of pilocarpine on iodopyracet and iodide accumulation by rabbit ciliary body preparations Invest Ophthal 5 378 1966

Results

The vascularity of the disc was diminished in all our cases according to the degree of cupping (Fig 1) Circumpapillary choroidal atrophy was a constant finding even in the youngest patient aged 36 and only in one of the patients circumpapillary atrophy could be attributed to myopia

Peripapillary atrophy of the pigmentepithelium as sign of impaired choroidal circulation (Fig 2) was characteristic in cases with marked cupping and visual field defects (Fig 3) The atrophic zone formed a distinct region in the centre of the fundus though not always circular The retinal arterioles were narrow in correspondence to the degree of arteriolar sclerosis Retinal radial peripapillary capillaries were visible in one case (Fig 4) showing severe changes of the capillary structure neovascularization and congestion This patient had severe macular degeneration and a i o pressure level of about 40 mm Hg before treatment

Discussion

Fluoresceinangiography of the fundus of glaucomatous patients may be technically difficult especially in longstanding cases with senile or secondary opa



Fig 1

Diminished vascularity of the optic disc and circumpapillary atrophy in a man aged 69 with chronic glaucoma The pre treatment pressure level was 40 mm Hg and an enlarged blind spot and a nasal step were found on perimetry

Material and Method

The present series (Table 1) consisted of 12 patients with chronic wide angle glaucoma and cupping of the disc. Patients with 1) a pre-treatment pressure level > 25 mm Hg, 2) pathologic diurnal curves and cupping of the disc were included in the series. When angiography was performed, 3) a pressure was ≤ 35 mm in all cases. Half of the patients were female and with one exception the patients were over 50 years of age. The visual fields were plotted using the Goldmann apparatus for kinetic perimetry. The central isopter 20° nasally using either test object I and intensity 2 or object 0 and intensity 3 was plotted using near correction and constant background illumination. None of the patients had diabetes, hematologic or severe hypertensive disease. Fluorescein angiography was performed at 2 sec intervals by the method formerly described by Rantta (1968).

Table 1
Data on 12 patients with wide angle glaucoma

Case	Age	Sex	The disc	Visual field
1	76	F	glaucomatous excavation	a part of temporal quadrant is left
2	73	F	glaucomatous excavation	a part of temporal quadrant is left
3	64	F	incipient glaucomatous excavation	an enlarged blind spot
4	36	F	incipient glaucomatous excavation	an enlarged blind spot
5	46	F	a temporal glaucomatous excavation	an enlarged blind spot
6	59	F	incipient glaucomatous excavation	normal
7	54	M	glaucomatous excavation	a Bjerrum scotoma
8	70	M	incipient glaucomatous excavation	normal
9	62	M	glaucomatous excavation	Bjerrum scotoma and nasal step
10	68	M	glaucomatous excavation	an enlarged blind spot and a nasal step
11	46	M	a temporal glaucomatous excavation	an enlarged blind spot
12	69	M	glaucomatous excavation	an inferior and temporal part of the field are left

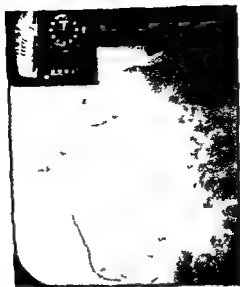


Fig 4

Fluorescence pattern of a woman aged 16 with untreated glaucoma and a pressure level of 40 mm Hg and macular degeneration. Marked visual field loss.

have been found in choroidal as well as retinal peripapillary circulation (Alterman & Henkind 1968 and Dollery 1968).

Hemodynamics of the ocular circulation has some special features. Because of the intraocular pressure venous capillary pressure is high approximately 2 mm Hg higher than the i.o. pressure. Elevated i.o. pressure of any kind increases therefore the pressure in the veins. The radial peripapillary capillaries being mainly veins seem to be very vulnerable to increased pressure. Fluorescein angiographic changes of these capillaries were visible only in one of our cases with additional macular degeneration. It might be concluded that the vascular lesion in glaucoma leading to nerve bundle lesion is choroidal and that only an arcuate angioscotoma seen early in glaucoma as well as in other conditions like papilledema (Raitta & Lannas 1969) can be produced by affection of the radial peripapillary capillaries. Juxta- and peripapillary atrophy of the pigment epithelium was a constant finding and was most distinct in cases with severe cupping and functional loss. Whether these changes are primary or secondary to elevated i.o. pressure is an interesting question. Changes of the posterior and anterior uveal circulation might well be parallel. This might be an explanation to the fact that glaucomatous changes may progrediate even if i.o. pressure levels are well controlled and to the so-called low tension glaucoma. The degree of papillary and peripapillary changes corresponded with the de-



Fig 2

Peripapillary atrophy in a man aged 62 with a typical nerve bundle defect of the visual field Pre treatment pressure level 30 mm Hg

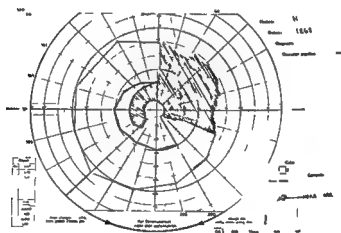


Fig 3

Visual field of patient described in fig 2

cities of the cornea lens and/or vitreous In Hayreh's (1967) study a diminished fluorescence of the disc was found to be typical No comments however were made upon peripapillary changes In experimentally elevated pressure changes

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A STUDY ON THE DISTRIBUTION OF ALKALINE PHOSPHATASE IN CERTAIN RETINAL LOCALES OF SNAKE AND VARANUS AND ITS FUNCTIONAL SIGNIFICANCE IN THE VISUAL PROCESSES

BY

H. B. TEWARI and H. R. TYAGI

Although histological accounts of reptilian eyes are available in the literature (Walls 1958) yet studies on the distribution of phosphatases and other enzymes on such retinae are lacking. There is only a solitary report on the distribution of cholinesterases retinae of turtle and lizards (Capurro *et al.* 1959). On the other hand other vertebrate eyes including humans have been extensively investigated from the point of view of distribution of phosphatases and other enzymes. Also the distribution of cholinesterases and non specific esterases in the retinae of some mammals has been adequately investigated (Esila 1963). The present contribution incorporates a detailed account of the distribution of alkaline phosphatase and discusses its metabolic roles in various retinal layers of snake and varanus. Further the distributive patterns in the two animals have been also compared.

Material and Methods

Eyes of snake and varanus obtained in living condition were cut into small pieces and were immediately fixed in 10% neutral formalin for periods vary

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gree of cupping and the severity of the visual field loss. Advanced visual field loss was found to be a typical nerve bundle loss whereas early loss seen as enlargement of the blind spot probably is an angioscotoma corresponding to the circulatory changes of the peripapillary area.

Summary

A fluorescein study of the papillary and peripapillary region in 12 patients with chronic wide angle glaucoma and cupping of the disc is presented.

Diminished vascularity of the disc and circumpapillary choroidal atrophy was a constant finding in the series. In advanced glaucoma with severe functional loss a peripapillary atrophic area was typical. Severe vascular changes not only of the disc but of the juxtapapillary and peripapillary zone indicated that a zonular arrangement of the choriocapillaries might exist.

References

- Altman M & Henkind P* Radial peripapillary capillaries of the retina. II Possible role in Bjerrum scotoma. *Brit J Ophthalm* 52: 26-31, 1968.
- Dollery C T, Henkind P, Kohner E & Paterson J W* Effect of raised intraocular pressure on the retinal and choroidal circulation. *Invest Ophthalm* 7: 191-198, 1968.
- Hayreh S S* Blood supply of the optic nerve and its clinical significance. *Acta Ophthalmologica* New Delhi 11: 94-119, 1962.
- Hayreh S S & Walker W M* Fluorescent fundus photography in glaucoma. *Am J Ophthalm* 63: 982-989, 1967.
- Michaelsson I C* Retinal circulation in man and animals. Charles C Thomas Publ. Springfield Ill, 1954.
- Raitta G & Vannas S* Radial peripapillary capillaries in oedema of the optic disc. Paper read at the Int Symp on Fluoresceinangiogr. Albi, June 9-14, 1969.

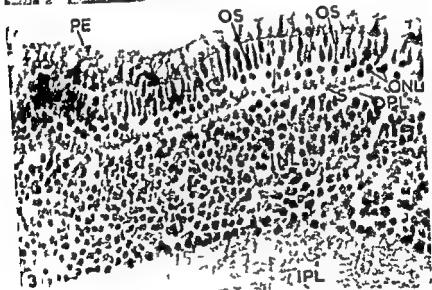
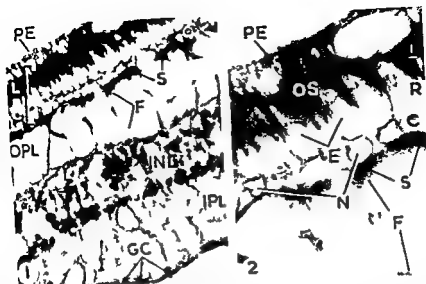


Fig 1

Retina of Snake Distinguish the layers - pigmented epithelium (PE) layer of rods and cones (LRC) Outer nuclear layer (ONL) synapses (S) Fibers (F) Outer plexiform layer (OPL) Inner plexiform layer (IPL) and ganglion cell (GC) $\times 430$

Fig 2

Higher magnification of Fig 1 Note the intense alkaline phosphatase activity in the outer segments of Rods and Cones (OS) Ellipsoid negative ellipsoid (E) and nuclear containing part (N) $\times 145$

Fig 3

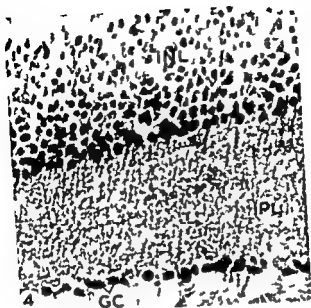
Retina of human Distinguish pigmented epithelium (PE) Distinguish positive layer of rod and cones (LRC) having positive outer segment (OS) and nuclei constituting outer nuclear layer (ONL) Positive synapses (S) in the outer most region of the negative outer plexiform layer (OPL) are also seen The latter is thinner than that of snake (compare OPL Fig 3 with OPL Fig 1) inner nuclear layer is thicker than that of snake's retina (compare INL Figs 1 and 3) $\times 550$

ing from 4 to 6 hours Paraffin sections 10 μ thick after brief washing in distilled water were processed through Gomori's technique for alkaline phosphatase (cf *Pearse* 1961) Suitable controls were also simultaneously made

Results

In our preparations, both in control and normal identical staining in the pigmented epithelium prevents us from considering this layer as one of the sites of alkaline phosphatase activity. However interesting results are provided by the layer of rods and cones (LRC Fig 1). In diurnal Colubrids to which the present material (*Ptyas mucosus*) belongs single and double types of cones are composed of outer segment ellipsoid and nuclear containing part (*Walls* 1958). Our preparations reveal that only the outer segments (OS Fig 2) are equipped with the enzymatic activity of a high order the ellipsoid (E Fig 2) and the nuclear containing part (N Fig 2) are totally negative. It is interesting however to mention here that acid phosphatase activity has been seen in human cone ellipsoid by *Lassel et al* (1964). The notable point which must be stressed here is that the nuclei of all the cones constituting the outer nuclear layer (ONL Fig 1) are totally negative (see also N Fig 2). In a variety of tissues the nuclei are invariably alkaline phosphatase positive by Gomori's technique - a condition believed by some workers (*Holt* 1959 1961 *Barka & Anderson* 1962 *Deane* 1963) to be artefactual in nature due to adsorption of lead ions or of lead or calcium phosphates by the nuclear sites even in the absence of any enzymic activity. In the present case the absence of the alkaline phosphatase staining in all the nuclei can be advanced as one of the convincing arguments to disprove the assumption that nuclear sites always absorb reaction products or some constituents of the incubating medium of Gomori's technique and reveal false sites of the enzymatic activity. In our experiments in spite of the presence of calcium ions all the nuclei of the rods and cones have failed to acquire staining. Thus we believe that the localization of alkaline phosphatase in nuclei wherever it is seen represents the factual localization of the enzyme and is not due to any preparative factor.

From the enzymatic point of view the other interesting sites besides the outer segments of the cones are the synaptic zones located at the bases of the cones in the outer most regions of the outer plexiform layer. These areas representing the synapses between fibers of the bipolar horizontal and other cells of the inner nuclear layer and the bases of the cones are provided with intense enzymatic activity in our preparations (S Figs 1 and 2). In the inner region of the outer plexiform layer (OPL Fig 1) which is mainly constituted by traversing fibers of neurons of other layer the enzymatic activity is com



5

Fig 4

Note the intensely positive Muller's fibers (arrows) running across the whole length of inner plexiform layer (IPL). Deeply stained ganglion cells (GC) are also seen

× 916

Fig 5

Distinguish a deeply stained positive zone at S above the positive ganglion cell (GC). The remaining inner plexiform layer is feebly stained (IPL). Further identify the positive nerve fibers (NF) emerging from the ganglion cells and the associated positive synapses (S). × 1165

pletely lacking e.g. in some instances total lengths of fibers negative in nature (Figs 1 and 2), are traceable across the outer plexiform layer. However the inner nuclear layer, composed of closely packed bipolar cells (amacrine Muller and other types of bipolar cells) is intensely positive for alkaline phosphatase (INL Fig 1). On the other hand the inner plexiform layer provides a very faint diffused reaction (IPL Fig 1). Further the ganglion cells (GC Fig 1) constituting the inner most zone of the retina and the nerve fibers possess intense enzymatic activity.

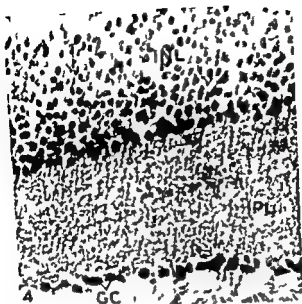
Varanus retina

The retina of *Varanus* monitor is essentially composed of the same layers as in the case of snake. Only three variations are seen – firstly both rods and cones are found, secondly the outer plexiform layer is greatly reduced and thirdly the inner nuclear layer is considerably thicker.

As in the case of the snake's retina the pigmented epithelium of *varanus* also reveals identical staining in control as well as in normal preparations. Consequently this layer from the enzymatic point of view has been excluded from consideration. The outer segments of both rods and cones in *varanus* are intensely positive for alkaline phosphatase activity (OS Fig 3) and in this respect resembles the staining seen in the outer segments of the cones of snakes (compare OS Figs 2 and 3). One significant departure in *varanus*'s retina from that of snake's retina however is that all the nuclei of the rods and cones composing the outer nuclear (ONL Fig 3) are invariably positive (compare ONL Figs 1 and 3). Such differences between the two retinæ then provide an interesting situation where we find that in spite of identical processing the nuclei in one case are negative and in other case positive. This gives an added support to our view that nuclear localization of alkaline phosphatase by Gomori's technique is not artifactual in nature as feared by some workers but reflects the real enzymatic make up of the nuclei which give such staining.

In the peripheral portions of the outer plexiform layer (OPL Fig 3) which is considerably reduced in *varanus* as compared to that of snake (compare OPL Figs 1 and 3) the synaptic zones (S Fig 3) at the bases of the rods and cones are positive for alkaline phosphatase activity. Thus we find that in both the retinæ such synapses are identically equipped with the enzymatic activity (compare S Figs 1, 2, 3). The remaining portion of the outer plexiform layer (OPL Fig 3) is devoid of the alkaline phosphatase activity.

The inner nuclear layer the zone much bigger than that of snake on the whole reveals enzymatic activity of a high order (INL Fig 3). The entire area is seen packed up closely by intensely positive neurons. In the inner plexiform layer an interesting observation relates to the positive fibers traversing the entire length of the area (arrows IPL Fig 4). These are probably Muller's fibers.



5

Fig 4

Note the intensely positive Muller's fibers (arrows) running across the whole length of inner plexiform layer (IPL). Deeply stained ganglion cells (GC) are also seen

$\times 816$

Fig 5

Distinguish a deeply stained positive zone at \parallel above the positive ganglion cell (GC). The remaining inner plexiform layer is feebly stained (IPL). Further identify the positive nerve fibers (NF) emerging from the ganglion cells and the associated positive synapses (S_1) $\times 1160$

Another very interesting situation seen in varanus retina relates to the area adjacent to the ganglion cells. This area (S Fig 5) is constituted by synapses located immediately above the ganglion cells and possesses enzymatic activity of a higher order than the remaining portion of the inner plexiform layer (IPL Fig 5). The inner most layer is composed of ganglion cells and amacrine cells. In our preparations these cells (GC Figs 4 and 5) have provided an intense enzymatic reaction. It is also very interesting to note that the fibers emerging from these cells and their synaptic contacts with extra retinal fibers (S1 Fig 5) possess enzymatic activity.

Discussion

In the present study the outer segments of rods and cones the highly sensitive parts where the light strikes first and initiates nervous excitation reveal intense alkaline phosphatase activity. In outer segments of rods and cones of pig, rat and mouse the alkaline phosphatase activity has been also described (Lessel *et al.* 1964). Now the question arises whether such enzymatic activity is in any way related to the initial visual processes undergoing in rods and cones? To seek a possible answer it is necessary first to understand that morphological and physiological conditions available in the outer segments of rods and cones. Electron microscopical studies reveal that such regions are composed of closely packed flattened saccules which are derived from the plasma membranes. In adult condition even some of the saccules remain connected with the plasma membrane throughout life in amphibian (Lanzavecchia 1960, Lasansky & De Robertis 1960, Yamada 1960, Moody & Robertson 1960, Brown, Gibbon & Wald 1963). Cohen (1961, 1963, 1964) also note such a connection in the cones of pigeon, grey squirrel and monkey. The details of the initial steps in visual stimulation occurring in outer segments is still undecided. There are two hypotheses – one believes that each saccule is a light sensitive receptor (Wald 1958) the other postulates that the whole outer segment is a photosensitive structure. Missotten (1965) remarks that a difference in potential and difference in the ionic distribution existing between the inside and outside of a saccule is responsible for starting the initial steps in visual stimulation. Brown *et al.* (1963) believe that the special structure of the rim of the flattened saccule plays a part in the conveyance of the stimulation. Since a saccule arises as a result of infolding of the plasma membrane a difference in ionic distribution as obtainable on the inner and outer sides of the plasma membranes is certainly expected on the inside and outside of the saccule as well since inside in infolded condition represents extracellular space and the outside the intracellular space. In other words a situation akin to the biochemical makeup of the plasma membra

nes on the outer and inner sides of the saccules is available in the outer segments of rods and cones and such structures are expected to possess the substances and the metabolic activities of the same type and of the same order as are available in and around the plasma membrane. Various types of phosphatases have been demonstrated at the neuronal and non neuronal plasma membranes (Pothstein & Meier 1948 Derrick *et al* 1953 Clarkson & Mats 1952 Tewari & Bourne 1967a, 1963a b 1964 Tewari & Sood 1969 Thakar & Tewari 1967 Tewari & Dabholkar 1968). In this context therefore it would be quite reasonable to expect the presence of alkaline phosphatase at the membranes of the saccules which are nothing but the modified form of the plasma membranes. Tewari & Bourne (1960a b 1961a b Tewari *et al* 1962c) in a number of studies have also demonstrated the presence of alkaline phosphatase other phosphatases and enzymes in another derivative of the plasma membrane namely the myelin sheath of sciatic nerve of rat the concentric rings of which are thought to arise from the plasma membranes in the same fashion as the membranes of the saccules (Adler 1965). In the plasma membranes of excitable tissues the role of sodium and potassium ions through the mediation of phosphatases has been also fairly well established in the creation of action potential (Danielli 1952 Tosteson *et al* 1961 Tewari & Bourne 1960a b 1961a b 1962c Pinner *et al* 1964) - particularly a phosphatidic acid cycle as a sodium carrier involving ATP and ATPase has been postulated by Hokin & Hokin (1961). ATPase activity has been also seen in the outer segments of the retinæ of many vertebrates (Lesser *et al* 1964). Since it has not yet been conclusively established whether ATPase is a simple enzyme or a combination of phosphokinase and a phosphatase (Whittam 1964) it can be suggested at the moment on the basis of present results that the phosphatases in general seem to be concerned with the permeability processes concerned with the ionic balances associated with creation of action potential. Also Tewari & Bourne (1962a, 1963a b 1964) have found identical pattern of localization of alkaline phosphatase and ATPase at the neuronal surfaces and the role of phosphatase have been linked with the permeability processes. The significance of energy phosphate compounds in active transport is also pointed out by the experiments in which application of such compounds on the inner membranes of red cells and nerve fibers revive the otherwise stopped active transport (Caldwell *et al* 1960a b Caldwell & Keynes 1957).

Against the background of these evidences our results demonstrating intense alkaline phosphatase activity in the zones of rods and cones possessing closely packed up structures derived from plasma membranes acquire considerable importance. Our observations become more interesting when we consider that the initial factors for the origin of the stimulus like the imbalances of Na and K ions similar to the situations seen around the nerve membranes evoking impulses are available also around each saccule. Since alkaline phosphatase is also

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Discussion

In the present study the outer segments of rods and cones the highly sensitive parts where the light strikes first and initiates nervous excitation reveal intense alkaline phosphatase activity. In outer segments of rods and cones of pig, rat and mouse the alkaline phosphatase activity has been also described (Liesel *et al* 1964). Now the question arises whether such enzymatic activity is in any way related to the initial visual processes undergoing in rods and cones? To seek a possible answer it is necessary first to understand that morphological and physiological conditions available in the outer segments of rods and cones. Electron microscopical studies reveal that such regions are composed of closely packed flattened saccules which are derived from the plasma membranes. In adult condition even some of the saccules remain connected with the plasma membrane throughout life in amphibian (Lanzavecchia 1960, Lasansky & De Robertis 1960, Yamada 1960, Moody & Robertson 1960, Brown, Gibbon & Wald 1963). Cohen (1961, 1963, 1964) also note such a connection in the cones of pigeon, grey squirrel and monkey. The details of the initial steps in visual stimulation occurring in outer segments is still undecided. There are two hypotheses – one believes that each saccule is a light sensitive receptor (Wald 1958) the other postulates that the whole outer segment is a photosensitive structure. Missotten (1965) remarks that a difference in potential and difference in the ionic distribution existing between the inside and outside of a saccule is responsible for starting the initial steps in visual stimulation. Brown *et al* (1963) believe that the special structure of the rim of the flattened saccule plays a part in the conveyance of the stimulation. Since a saccule arises as a result of infolding of the plasma membrane a difference in ionic distribution as obtainable on the inner and outer sides of the plasma membranes is certainly expected on the inside and outside of the saccule as well since inside in infolded condition represents extracellular space and the outside the intracellular space. In other words a situation akin to the biochemical makeup of the plasma membra

concerning specific and non specific cholinesterases in green and sand lizards and European turtle. In green lizard retina there is no activity of specific cholinesterase in any layer except in inner plexiform layer and moderate activity in ganglion cells. In sand lizard however there is moderate activity in outer plexiform layer, amacrine cells and intense activity in inner plexiform layer and ganglion cells. In European turtle there is no specific cholinesterase activity in outer and inner segments of visual cells. Thus it is seen that the outer segments of snake and varanus which possess alkaline phosphatase activity as evidenced in the present study are devoid of specific cholinesterase activity. The inner segment of snake is negative for alkaline phosphatase and thus resembles the retinae of green and sand lizards as far as specific cholinesterase localization is concerned. However in the inner segments of varanus there is a moderate activity for alkaline phosphatase - this compares favourably with the absence of cholinesterase activity in the same layer of green and sand lizards. The outer nuclear layer is positive for specific cholinesterase in European turtle. In our results in snake the layer is negative for alkaline phosphatase and in this respect resembles the similar layers in green and sand lizards which are negative for specific cholinesterases. The outer nuclear layer of varanus is alkaline phosphatase positive which in turtle also possess specific cholinesterase activity. In our material only the fiber traversing the outer plexiform layer demonstrates feeble alkaline phosphatase activity otherwise the layer is generally negative. In turtle the same layer possesses moderate specific cholinesterase activity which is negative for this enzyme in green and sand lizards. The inner nuclear layer of turtle possesses moderate activity for specific cholinesterase and the same layers in green and sand lizards are negative. The ganglion cells in European turtle as well as in green and sand lizards are positive for cholinesterase. These cells as already mentioned are positive for alkaline phosphatase in our materials. In all the cases Capurro *et al* (1959) find complete absence of cholinesterases in the nerve fibers emerging from the ganglion cells. In our study such fibers are positive for alkaline phosphatase.

Summary

The study incorporates a detailed consideration on the distribution of alkaline phosphatase in certain retinal localities of snake and varanus and discusses the functional significance of the enzyme in the visual processes. Although most of the constituents of the retinae like ganglion cells and other types of neurons have provided enzymatic activity of varying degree but the most interesting sites from the enzymatic point of view are the outer segments and synapses located at the bases of cones and rods and also above the ganglion cells. A

present in these regions it seems quite reasonable to suggest that changes in the permeability through the mediation of alkaline phosphatase may be the factors for initial stimulation in the outer segments. The present light microscopical study, however, imposes on us a restriction to pin point the exact locale of alkaline phosphatase activity in the outer segments. But such a handicap is unlikely to undermine our interpretation relating to the significance of alkaline phosphatase since both the views involving either the whole outer segment or only saccules are invoked at present. Even if it is assumed that only saccules are concerned with the propagation of impulses then it may be pointed out that such structures fill up the outer segments so closely and completely that hardly any non saccular area is left and due to such tightly piled up alkaline phosphatase-positive saccular membranes the whole outer segment in a light microscopical picture would appear as if the enzymatic activity is present throughout the outer segment.

The other interesting aspect of the present observations is the location of the enzymatic activity at various synaptic sites particularly at the bases of rods and cones and in the zone above the ganglion cells. *Sjostrand* (1955) has clearly demonstrated that the dendrites of the cells penetrate and digitate into the enlarged terminal endings of the rods and cones to effect intimate synaptic contacts. It is exactly at such sites that our results demonstrate intense alkaline phosphatase activity. In a number of studies *Tewari & Bourne* (1962b, 1963c) have suggested that alkaline phosphatase is concerned with the permeability processes across the synaptic membranes and we believe that the enzyme is playing the same role at these sites as well. The same holds true for the synaptic contacts located above the ganglion cells.

Walls (1963) has linked Muller's fibers to riverts which run through the whole thickness of the retina proper and bind its layer together and occupy a surprising amount of the total volume of the retina. Although previously the Muller fibers were thought to be simply supporting in nature recent evidences based on the electrophysiological response of flashes of light (*Stavitsky et al* 1961) suggest that the fibers are associated with the metabolic and neuroregulatory roles. In our preparations such fibers reveal alkaline phosphatase activity and therefore it is possible that the enzyme may be playing its role in metabolic and neuroregulatory processes occurring in these fibers.

Regarding the significance of the distribution of alkaline phosphatase in ganglion cells and other neurons it may be briefly mentioned that the enzyme seems to be concerned with protein synthesis occurring in these cells as has been discussed earlier by us (*Tewari & Taga* 1967).

It seems interesting to see whether the alkaline phosphatase positive locales in our materials are also equipped with other enzymes in retinas of snake, varanus and other animals. As already mentioned there is hardly any enzymatic study in the retinas of snake and varanus except that of *Capurro et al* (1959).

- 16 *Fernande Moran H* Science 1959 129 1784 Cited in Ch The structure of the rabbit retina as revealed by electron microscopy In The rabbit in Eye research Charles C Thomas Publisher Springfield Illinois
- 17 *Fernandez Moran H* Fine structure of the Biological lamellar systems In Bio physical Science A Study programme Ed Oncley L L J Wiley & Sons N Y 1959 319 30
- 18 *Fernande Moran H* N Y Acad Sci Ann 1960 85 689 Cited in Ch The structure of the rabbit retina as revealed by electron microscopy In The rabbit in Eye research. Charles C. Thomas Publisher Springfield Illinois
- 19 *Hokin L E & Hokin M R* Nature 1961 149 563 Cited in Ch The Interdependence of Metabolism and active transport (Whittam R) In The cellular functions of Membrane transport Ed J F Hoffmann Prentice Hall Inc Englewood Cliffs New Jersey
- 20 *Arinsky A* The lipoprotein nature of rhodopsin Arch Opthl 1958 60 688
- 21 *Arinsky A* The enzymatic esterification of vitamin A J Biol Chem 1958 239 881
- 22 *Lan avecchia G* Ultrastructura dei coni e dei bastoncelli nella retina di *Xenopus laevis* Arch Ital Anat Embriol 1960 6 417 35
- 23 *Lasansky A & De Robertis E* Electron microscopy of retinal photoreceptors the use of chromation following formaldehyde fixation as a complementary technique to osmium tetroxide fixation J Bioph Biochem Cytol 1960 7 493 94
- 24 *Leisell S & Kuwabara T* Arch Ophthalmol (Chicago) 1964 Vol 71 6
- 25 *Muscatell L* The ultrastructure of the Human Retina Arsia Uitgaven N V Brussel 1965 11 184
- 26 *Moody M F & Robertson J D* The fine structure of some retinal phot receptors J Bioph Biochem Cytol 1960 7 87 92
- 27 *Pearse A G E* Alkaline Phosphatases In Histochemistry Theoretical and applied II edition J & A Churchill Ltd London 1961 385 430
- 28 *Pinner B Dawson John F & Campbell James B* Alkaline Phosphatase in Peripheral Nerves Reprinted from Science 1964 Vol 15 No 1935 pp 936 38
- 29 *R thestein A & Meier H* The relationship of the cell surface to metabolism J Cell Comp Physiol 1948 37 17 95
- 30 *Sjostrand F S J* Appl Phys 1953 24 1492 In Submicroscopic Morphology of the synapse by Eduardo De Robertis. Int Rev Cytol 1959 8 61 96
- 31 *Sjostrand F S & Nilsson S E* Ch The structure of the rabbit retina as revealed by electron microscopy In The Rabbit in Eye Research J H Prince Ed Charles C Thomas Springfield Illinois USA 1953
- 32 *Stastiehm G Laufer M Mitrav G Fatchenahd R Vallecalle E & Villegas J* Clial control of neuronal network and receptors In The visual system Neuro physiology and Psychophysics Ed R Jung and H Kornhuber Berlin Springer Verlag 1961 445 456
- 33 *Tewari H B & Bourne G H* Neurokeratin network of the peripheral nerve fiber myelin sheath as a centre of metabolic activity Nature 1960 186 645 46a.
- 34 *Tewari H B & Bourne G H* Histochemical localization of specific and non specific cholinesterases and simple esterases in myelinated nerves Exper Cell Res 1960 1 45 45b
- 35 *Tewari H B & Bourne G H* The structure and biochemical identity of the neurokeratin network of myelinated nerve fibers Bibl Anat. 1961 9 111 127a.

detailed consideration on the possible roles of alkaline phosphatase in the outer segments has been made with reference to the initial visual processes occurring in these areas. The significance of the distribution of alkaline phosphatase at the synaptic sites has been also discussed with reference to the transmission of impulses.

References

- 1 Adler F H Physiology of the eye. 4th edition The C V Mosby Company Saint Louis 1963
- 2 Barka & Anderson On the demonstration of Acid Phosphatases J Histochem Cytochem 1962 10 74 In Nuclear location of phosphatase activity Fact and Artifact by Helen Wendler Deane J Histochem and Cytochem 1963 11 443 44
- 3 Brown P A Gibbons I R & Wald G The visual cells and visual pigments of the mud puppy Necturus J Cell Biol 1963 1:9 19 106
- 4 Caldwell P C Hodgkin A L Keynes R D & Shaw T I J Physiol London 1960 152 561 a In Alkali Cation Transport by Wilbrandt W Int Rev Cytol Ed Bourne G H & Danielli J F Acad Press N Y London 1960 15 03 19a.
- 5 Caldwell P C Hodgkin A L Keynes R D & Shaw T I J Physiol London 1960 152 591 b In Alkali Cation Transport Wilbrandt W Int Rev Cytol Ed Bourne G H & Danielli J F Acad Press London 1960 15 203 19
- 6 Caldwell P C & Keynes R D J Physiol London 1954 151 12 In Alkali Cation Transport Wilbrandt W Int Rev Cytol Ed Bourne G H & Danielli J F Acad Press N Y London 1962 13 203 19
- 7 Capurro S Zaccheo E & Viale G Accorche istochimiche sulla attivita colinesterasica nella retina di rettili Boll Soc ital biol sper 1959 35 1 609 10
- 8 Clarkson F M & Maicis M J Physiol London 1952 116 112 In Best J B Ch Enzymic Processes in Cells Int Rev Cytol Ed Bourne G H & Danielli J F Acad Press N Y London 1960 129 131
- 9 Cohen A I Some preliminary electron microscopic observations of the outer receptor segments of the retina of the Macaca rhesus In The structure of the eye Ed G K Smelser Acad Press N Y 1961 p 151 53
- 10 Cohen A I The fine structure of the visual receptors of the pigeon Exp Eye Res 1963 2 88 97
- 11 Cohen A I Some observations on the fine structure of retinal receptors of the american gray squirrel Invest Ophthalm 1964 3 193 216
- 12 Danielli J F Symp Soc Exptl Biol 1952 6 1 In Alkaline Phosphatase in Peripheral Nerves Pinner H John F Davison James B Campbell Science 1964 Vol 15 No 1935 pp 936 38
- 13 Deane H W Nuclear location of phosphatase activity Fact or Artifact? J Histochem Cytochem 1963 11 443 44
- 14 Derrick M J Miller R E & Sevag M G Federation Proc 1953 12 196 In Best J B Ch Enzymic Processes in Cells Int Rev Cytol Eds Bourne G H & Danielli J F Vol 9 1960 Academic Press N Y
- 15 Esila R Histochemical and Electrophoretic properties of cholinesterases and non specific esterases in the retina of some mammals including man Act Opth Supp 1963 7:9 105

SPONTANEOUS EXTRUSION OF SUBCONJUNCTIVAL CYSTICERCUS

BY

M VENKATARAMI REDDY O M SATYENORAN
and K SIVARAMAKRISHNA

Introduction

Cysticercus cellulosae is the larval form of *Taenia Solium* an intestinal parasite. Man is usually a definitive host of *Taenia Solium* but occasionally becomes an intermediate host harbouring the bladder worm stage known as *cysticercus cellulosae*. The mode of infestation is by taking food and water contaminated with faecal matter containing ova. A man harbouring the adult worm may autoinfect himself from unclean personal habits. The envelope of the ova is dissolved in the upper intestinal tract releasing the embryo which by their hooklets penetrate into the wall of the intestine and enter the vascular and lymphatic plexus. They are carried and get filtered in the muscles and viscera of the body. They finally develop into *cysticercus cellulosae* a bladder worm which is composed of a head, neck and a caudal vesicle. The common sites are the eyes, brain, skin and muscles. It gets calcified in a period varying from 5 years to 12 years after the death of bladder worm (Chatterjee 1967).

Ocular cysticercosis is not a rare disease at Hyderabad, Andhra Pradesh. 32 cases of ocular cysticercosis were noticed from January 1960 to April 1969 in our Institute. Of which there were 23 cases from epibulbar region, 2 from palpebral conjunctiva, 3 from the fornices, one each from the lid, orbit, vitreous and anterior chamber. Cases of spontaneous extrusion of subconjunctival cysticercus has not been reported previously to our knowledge. In the present case

- 36 *Tewari H B & Bourne G H* New morphological identity and functional significance of the neurokeratin network of myelinated nerve fibers *Pathologie Biologie Paris* 1961 919 924b
- 37 *Tewari H B & Bourne G H* Histochemical evidence of metabolic cycles in spinal ganglion cells of rat *J Histochem Cytochem* 1962 10 49 64a
- 38 *Tewari H B & Bourne G H* Absence of specific cholinesterases from cerebellar synaptic function and localization of other enzymes *Exptl Cell Res* 1967 7 173 77b
- 39 *Tewari H B Quinton Cox R & Bourne G H* Further observations on the neurokeratin network of peripheral nerves *Exptl Cell Res* 1962 28 516 87c
- 40 *Tewari H B & Bourne G H* On the topographical differences in the localization of certain enzymes in trigeminal ganglion cells of rat *Experientia* 1963 19 793 40a
- 41 *Tewari H B & Bourne G H* Histochemical studies on the localization of adenosine triphosphatase in the cerebellum of the rat *J Histochem Cytochem* 1963 11 246 57b
- 42 *Tewari H B & Bourne G H* On the histochemical demonstration of alkaline and acid phosphatase and simple esterase in the neurons and bouton terminaux of the cerebrum of rat *J Histochem Cytochem* 1963 11 116 18c
- 43 *Tewari H B & Bourne G H* Histochemical studies on the distribution of alkaline and acid phosphatases and 5 nucleotidase in the trigeminal ganglion cells of rat *Acta Histochemica* 1964 17 197 207
- 44 *Tewari H B & Dabholkar A S* Histochemical studies on the distribution of alkaline and acid phosphatases amongst the constituents of the abdominal and thoracic ganglia and the nerve cord of *Periplaneta americana* *Acta Histochemica* 1968 Bd 30 5 350 363
- 45 *Tewari H B & Sood P P* Histochemical studies on the distribution of alkaline and acid phosphatases amongst the constituents of the various layers of olfactory lobe of rat *Acta Anatomica* 1969 72 276 303
- 46 *Tewari H B & Tyagi H R* On the Alkaline Phosphatase Activity amongst the Constituents of the Eye of *Calotes versicolor* in Light and Dark Environments *Exptl Eye Res* 1967 7 200 204
- 47 *Thakar D S & Tewari H B* Histochemical studies on the distribution of alkaline and acid phosphatases amongst the neuron of the cerebellum of spinal and trigeminal ganglia of bat *Acta Histochem* 1967 28 359 367
- 48 *Tosteson D C Moulton R H & Blaustein M P* *Federation Proc* 1961 20 133
In Alkaline phosphatase in Peripheral nerves by Pinner B et al *Science* 1964 Vol 145 No 3635 936 38
- 49 *Wald G* Photochemical aspects of visual excitation *Exp Cell Res* 5 Suppl 1958 389 410
- 50 *Walls G L Ch* The Eyes of reptiles In *The Eye in Evolution* Ed Duke Elder S Henry Kimpton London 1958
- 51 *Walls G L* The vertebrate eye and its adaptive Radiation Hafner Publishing Company New York 1963 p 48
- 52 *Whittam R* The Interdependence of Metabolism and active Transport In *The cellular Functions of Membrane transport* Ed Hoffman J F Prentice Hall Inc Englewood Cliffs New Jersey 1964
- 53 *Yamada E* Observations on the fine structure of Photoreceptive elements in the vertebrate eye *J Electromicr (Jap)* 1960 9 1 14



Fig 2
Spontaneous extrusion of the cyst - last phase



Fig 3
Hot micrograph of cysticercus cellulosae $\times 80$ enlarged four times

Summary

37 cases of ocular cysticercosis were seen from January 1960 to April 1969 at the Institute of Ophthalmology Hyderabad. A rare case of spontaneous extrusion of parasite from the subconjunctival space is reported.

reported below the parasite came out spontaneously through the conjunctiva without any surgical intervention. Probably a break was formed in the conjunctiva, over the parasite due to necrosis.

Case Report

A Hindu girl aged 5 years came to the Out patient Department on 20.12.1968 with her parents with a complaint of swelling and redness in right eye which was accidentally discovered 5 days ago. There was no history of injury to the eye. On examination of right eye the lids were found to be normal. A centrally oval reddish swelling was noticed in the upper nasal quadrant a few millimetres away from the limbus. The conjunctiva was tense and congested over the swelling. Swelling could not be moved over the underlying sclera. Both the eye balls were found to be normal. The case was diagnosed as subconjunctival cysticercosis.

While taking the photograph the parasite began to come out through a small opening from the centre of the swelling. In a matter of 10 minutes the whole parasite came out with undulating movements (Fig 1 & 2) on its own accord leaving behind an empty subconjunctival pocket. The parasite by its macroscopic appearance showed all features of *Cysticercus cellulosae*. The conjunctival wound healed in a few days leaving no residual swelling. Histopathological examination of the cyst confirmed the diagnosis of *Cysticercus cellulosae* (Fig 3).

Discussion

The diagnosis of the condition was made early by its site, clinical features and by the age of the patient. But the most important and rare manifestation was its spontaneous extrusion of the parasite from the subconjunctival space.



Fig 1
Spontaneous extrusion of the cyst

*From Odense County and City Hospital Eye Department
(Chief P M Møller M D)*

DIVERGENCE PARALYSIS

BY

P M MØLLER

In neuro ophthalmological diagnosis an exact assessment of the restriction in ocular motility is often a decisive factor

During a period of 4 years we have seen 4 patients with motility disturbances which have been classified as divergence paralysis. The complaints were consistent. A sudden onset of diplopia for distance with a constant distance between the images whereas no diplopia was present at close and at reading with approx 30 cm.

Cases of this nature have not previously been reported in Scandinavian ophthalmological literature. The case histories will be reported below and discussed in connection with a review of previous foreign publications on this subject.

Since *Parinaud* in 1883 reported the first case of divergence paralysis it has been discussed at intervals whether in fact there is a centre for active ocular divergence.

From a phylogenetic point of view it might be imagined that a divergence centre would develop as the antagonist of a convergence centre. *Bruce* (3) has been one of the most ardent proponents of the view that divergence paralysis must be due to an affection of a given active divergence centre.

This theory has found support in the experiments of *Adler* (1). Conducting electrical impulses from human lateral rectus muscles he found these impulses to become intensified in immediate connection with divergences. He assumed that this increase in tonus issued from a divergence centre. Divergence has been induced in monkeys by stimulating the frontal cerebral cortex but this has not been possible in man.

References

- Chatterjee K D* 1967 *Parasitology* p 111
Duke Elder S (1965) *System of Ophthalmology* London Henry Kimpton p 473 475
Rao A V N & Satyendran O M (1967) *Arch Ophthalmology* p 249 255
Reddy P S & Satyendran O M (1964) *Amer J Ophthalmology* p 57 664

II SRP 210131

A male aged 37 with a history of complaints through 2 years in the form of periodical pain in the cervical spine towards the cranial base accentuated on turning the head. One year ago he had suddenly developed convergent strabismus with blurred vision and diplopia of a few days duration. Still shooting pain at the back of the neck at times with slight dysphagia. Shortly before admission again sudden permanent convergent strabismus with diplopia.

Visual acuity $\frac{6}{6}$ in both eyes emmetropia

Alternating convergence strabismus without restriction of motility and without nystagmus. At a distance of 3 m uncrossed double images abolished by prism 20 p d base out. The double images were of the same distance when gazing to the right and left. At 30 cm fusion without any movements of adjustment. Caloric test by the Hallpike method. Normal reactions with full abduction to both sides.

Ophthalmoscopic appearances normal no papilledema

Tomography revealed a large rhinopharyngeal tumour extending into the sphenoid sinus and destroying the dorsum of the sella and right down to the foramen magnum. Biopsy from the rhinopharynx failed to show definite tumour.

Autopsy revealed a large tumour at the base of the skull invading the sphenoid bone (rhinopharyngeal carcinoma).

III LSR 060459

A boy aged 6 years who for the past 6 months had been falling incessantly and had sustained several cranial traumas. According to his mother the boy had changed mentally and now had spells of fear. She had several times observed convergence which had again disappeared. Constant strabismus during the past two weeks before admission.

Visual acuity $\frac{6}{6}$ in both eyes emmetropia

Severe convergent strabismus completely free motility. No nystagmus. Reported constant uncrossed diplopia at 1 m when tested with red glass. Fusion at 15 cm and fusion at 6 m with a prism 30 p d base out.

Ophthalmoscopy revealed incipient papilledema on both sides.

Ventriculography showed a space filling lesion in the pons presumably a glioma. This was confirmed at operation.

Post mortem examination of the brain showed the tumour to be an astrocytoma of the pons.

IV EOM 140333

A female aged 35. During the past 2 years she had been suffering from occipital headaches. In addition she experienced difficulty in controlling her left arm and sudden twitches of the left leg. Two weeks before she was seen here she developed diplopia for distance most pronounced when she was tired.

When first seen, she did not have diplopia within 1 metre. Motility entirely normal. No nystagmus.

Visual acuity $\frac{6}{6}$ in both eyes emmetropia

Ophthalmoscopy showed bilateral papilledema of 4+ dioptries.

A few days later we observed ocular movements that might indicate bilateral abducens paresis with distinctly reduced motility.

After examination 7 months after the onset of the symptoms and signs and one week after the abducens paralysis had been observed again showed normal motility in all directions but the red glass test at 3 m as well as examination in the synoptophor. In Zeiss position showed uncrossed diplopia with the same distance between

Scobee & Green (11) have suggested that there is a vergence centre in the form of a convergence centre only "since exophoria and esophoria behave not as independent entities but rather as varying degrees of the same entity"

Chamlin & Davidoff (5) collected 15 cases of divergence paralysis. Of these patients 14 had elevated intracranial pressure. Eight were found to have tumours of the posterior fossa whereas in 7 no definite tumours were demonstrable. These authors therefore, suggest that despite the absence of papilledema patients with divergence paralysis should be suspected of elevated intracranial pressure.

In a paper on bilateral abducens paralysis *Bedrossian* (2) set up strict criteria for classifying a case as divergence paralysis. Watching ocular movements is not enough. The abduction has to be measured, and in pure cases (i.e. in the absence of 6th nerve palsy), it must exceed adduction by 10° .

According to *Bedrossian's* studies the abduction is 60° (measured as a normal field of fixation).

Nystagmus must not occur in the extreme positions if a case is to be diagnosed as divergence paralysis as this is taken to mean that the muscle is paretic.

In *Bedrossian's* opinion many reported cases of divergence paralysis have not been pure while on the other hand a number must have been overlooked considering the modest space devoted to divergence paralysis in the neuro ophthalmological literature.

The etiology of divergence paralysis is unknown. It has been observed in cases of poisoning, infections, disseminated sclerosis (hypoxic states) and in the presence of elevated intracranial pressure (*Chamlin & Davidoff*).

Case Reports

I N A M 160546

A male aged 19. Through the past year he had been suffering from diffuse headaches and occasional diplopia. For the past few months constant diplopia for distance. Stated that he could read without difficulty.

Visual acuity 6/6 in both eyes emmetropia.

At 3 m esotropia of 20 prism dioptres. No movement of adjustment, orthophoria at 30 cm. At 20 cm distinct exophoria.

Reported uncrossed diplopia with the same distance between the images at 4 m to the sides as well as up and down. In extreme positions delicate nystagmus.

Ophthalmoscopy showed papilledema at 1 dioptre in both eyes.

Ventriculography revealed a tumour in the posterior cranial fossa.

Operation disclosed a tumour suggesting a medulloblastoma in the pons. Estimated length 6.7 cm, transverse diameter approx 5 cm. The tumour did not involve the 4th ventricle. Part of the right cerebellar hemisphere and tonsil were removed. The tumour was infiltrating the brachium pontis.

Histological diagnosis Medulloblastoma.

Died in his home. No post mortem examination of the brain.

II SRP 710131

A male aged 37 with a history of complaints through 2 years in the form of periodic pain in the cervical spine towards the cranial base accentuated on turning the head. One year ago he had suddenly developed convergent strabismus with blurred vision and diplopia of a few days duration. Still shooting pain at the back of the neck at times with slight dysphagia. Shortly before admission again sudden permanent convergent strabismus with diplopia.

Visual acuity 6/6 in both eyes emmetropia

Alternating convergence strabismus without restriction of motility and without nystagmus. At a distance of 3 m uncrossed double images abolished by prism 20 Δ d base out. The double images were of the same distance when gazing to the right and left. At 30 cm fusion without any movements of adjustment. Caloric test by the Hallpike method. Normal reactions with full abduction to both sides.

Ophthalmoscopic appearances normal no papilledema

Tomography revealed a large rhinopharyngeal tumour extending into the sphenoid sinus and destroying the dorsum of the sella and right down to the foramen magnum.

Biopsy from the rhinopharynx failed to show definite tumour.

Autopsy revealed a large tumour at the base of the skull invading the sphenoid bone (rhinopharyngeal carcinoma).

III LSR 060459

A boy aged 6 years who for the past 6 months had been falling incessantly and had sustained several cranial traumas. According to his mother the boy had changed mentally and now had spells of fear. She had several times observed convergence which had again disappeared. Constant strabismus during the past two weeks before admission.

Visual acuity 6/6 in both eyes emmetropia

Severe convergent strabismus completely free motility. No nystagmus. Reported constant uncrossed diplopia at 1 m when tested with red glass. Fusion III 15 cm and fusion at 6 m with a prism 30 Δ d base out.

Ophthalmoscopy revealed incipient papilledema on both sides.

Ventriculography showed a space filling lesion in the pons presumably a glioma. This was confirmed at operation.

First post mortem examination of the brain showed the tumour to be an astrocytoma of the pons.

IV EOM 140833

A female aged 35. During the past 2 years she had been suffering from occipital headaches. In addition she experienced difficulty in controlling her left arm and sudden twitchings of the left leg. Two weeks before she was seen here she developed diplopia for distance most pronounced when she was tired.

When first seen, she did not have diplopia within 1 metre. Motility entirely normal. No nystagmus.

Visual acuity 6/6 in both eyes emmetropia

Ophthalmoscopy showed bilateral papilledema of 4.5 dioptres.

A few days later we observed ocular movements that might indicate bilateral abducens paresis with distinctly reduced motility.

At the examination 7 months after the onset of the symptoms and signs and one week after the abducens paralysis had been observed again showed normal motility in all directions but the red glass test at 3 m as well as examination in the synoptophore. Zero position showed uncrossed diplopia with the same distance between

the images in all directions Simultaneous perception and fusion at + 96 prism dioptres in the synoptophore and when examined at 20 cm

Ventriculography failed to show any definite abnormality

Right sided carotid angiography gave rise to a suspicion of a space filling lesion in the right hemisphere

The patient developed a severe mental disorder and committed suicide

Post mortem examination of the brain revealed an astrocytoma in the semioval centre in the right parietal region extending down towards the basal ganglia and through the corpus callosum towards the left side Brain stem and cerebellum normal The cut sections showed no abnormalities

Histological diagnosis Astrocytoma primarily affecting the right parietal region

All our 4 patients were fully awake and cooperative when examined

All were examined both with and without cycloplegia The angle of deviation did not change in complete paralysis of accommodation

Discussion

Our Cases I II and III had what I should call pure divergence paralysis

Case I had delicate nystagmus in extreme abduction to both sides I cannot accept Bedrossian's view that this is a sign of abducens paralysis when considering how often delicate nystagmus in extreme lateral gaze is found in normals

All our patients had confirmed tumours of the posterior fossa either in the pons or else as in Case II neoplastic masses infiltrated the cranial base as far as the sphenoid bone

Godtfredsen (7) never observed divergence paralysis among 240 patients with malignant tumours of the rhinopharynx

Our Case IV differed somewhat from the others When first seen she did not arouse any suspicion of divergence paralysis At 1 m there was no diplopia in the differentiated red glass test

A few days later however there was distinct limitation of abduction to both sides and in another week we found at 3 m distinct uncrossed diplopia which disappeared at 20 cm

In my opinion such a transient abducens paralysis could not rule out divergence paralysis in our Case IV cf *Walsh Clinical Neuro ophthalmology* (17)

We found definite divergence paralysis repeatedly but the varying transient limitations of abduction I interpret as mild abducens paresis subsequent to acute elevation of intracranial pressure Not uncommonly such paresis is seen in conditions involving elevated intracranial pressure As already mentioned there was bilateral papilledema of 4.5 dioptres

Our 4 patients had the following findings in common

- (1) Diplopia uncrossed for distance
- (2) They volunteered the information that at close they were not bothered by diplopia
- (3) A malignant intracranial tumour of the posterior fossa as the underlying cause

On this basis nothing can be concluded concerning the cause of the divergence paralysis except that pressure upon or against the brain stem must have been contributory but the exact localization of a presumed divergence centre cannot be deduced

The pons and the midbrain must be the site to look for the cause of the disease (int. al. Lyle (9)). It is of less importance to ascertain whether the lesion affects a given centre or else the posterior longitudinal fascicle or the medial longitudinal fascicle. It must be admitted that the intimate association between the oculomotor trochlear and abducens nuclei in coordinating ocular movements must be extremely vulnerable by a tumour in the pons and midbrain

On the whole the problem concerning divergence paralysis remains unsolved. It is given little attention in neuro ophthalmological diagnosis. In the event of a suddenly arising convergent squint especially in patients with neurological signs examination for this peculiar anomaly may be done. In most instances the differential diagnosis ought to be easy if only the patients are able to co-operate

Definite criteria of the diagnosis must be

- I Acute onset of homonymous permanent diplopia with a constant distance between the images in all positions especially in the horizontal plane
- II Esotropia for distance fusion at approx. 25-30 cm

Frequently we are apt to assume merely that a previously latent convergence due e.g. to a trauma has become manifest. Without performing the necessary diplopia test together with a fusion test at about 25-30 cm it is not possible to arrive at the correct diagnosis viz. divergence paralysis

A situation which may simulate divergence paralysis is esotropia arising as a result of contracture of the internal rectus muscle during the course of long lasting abducens paralysis. During the remission and upon return of normal abducens function the patient may exhibit esotropia with constant uncrossed double images for distance. According to Bynke (4) this is not entirely rare especially not in young children

It is also of importance in order to arrive at the diagnosis that any patient complaining of diplopia should be examined not only by the usual conventional differentiated red glass test within about $\frac{1}{2}$ m. Divergence paralysis usually does not manifest itself in uncrossed diplopia until at a distance of perhaps up to 5 m

Patients having convergence spasms and divergence insufficiency which may simulate divergence paralysis are often patients without serious neurological

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*From the Eye Department Odense County and City Hospital
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MEDIASTINOSCOPY WITH LYMPH NODE BIOPSY CARRIED OUT IN PATIENTS WITH ENDOGENOUS UVEITIS OF UNKNOWN ETIOLOGY

BY

VAGN NORDENTOFT M D and POUL MARTIN MØLLER M D

The presumed etiology of endogenous uveitis has varied very considerably throughout the times

Kaufmann (70) wrote in 1966: The main problem in the diagnosis of uveitis is that it is almost never possible to find the cause in a given case

In the last 15-20 years the interest in sarcoidosis as an etiological factor has been increasing, but in spite of the numerous biopsy methods that are available in suspected sarcoidosis this diagnosis is only rarely obtained in cases of endogenous uveitis. The frequency of sarcoidosis in different surveys is shown in Table 1. It is in the literature generally stated that the frequency is approximately 4 per cent.

The results of the present investigation are suggestive of a constant localization of sarcoid granuloma in the mediastinal lymph nodes in sarcoidosis (18).

In 1959 *Carlens* (15) described mediastinoscopy, a method which permits exploration of the superior mediastinum by palpation, inspection and biopsy. This

Read in part before the Danish Ophthalmological Society, Copenhagen, March 19th 1966.

The mediastinoscopies were performed at the department of Thoracic Surgery, Odense County and City Hospital. The histological studies were carried out at the Pathological Institute, Odense County and City Hospital. This study was supported by the Fundation for Medical Research performed at the hospitals on Funen.

Reprint requests to the Eye Department, Odense County and City Hospital, 5000 Odense, Denmark (Dr Møller).

Received February 1970

diseases, whereas patients with divergence paralysis should always be thoroughly studied as the sign is usually one in the symptom complex of a brain tumour

Summary

Four patients with signs of divergence paralysis are analysed. The author emphasizes the importance of a careful examination for diplopia for distance as well as for near in patients with sudden onset of convergence strabismus.

In all our four cases intracranial tumours were the underlying cause. Convergence spasms which may simulate divergence paralysis often represent a condition in which no neurological signs are manifest.

References

- 1 Adler F H Review of Convergence and Divergence Mechanisms Amer Orthop J 6 67 70 1956
- 2 Bedrossian E H Bilateral Sixth nerve Paresis Amer J Ophth 45 417 423 1958
- 3 Bruce G M Ocular Divergence its Physiology and Pathology Arch Ophth 13 639 660 1935
- 4 Byrke Hans Personal Communication 1969
- 5 Chamlin M & Davidoff L M Divergence Paralysis with increased Intracranial Pressure Arch Ophth 46 145 147 1951
- 6 Cogan D G Neurology of the Ocular Muscles Springfield Thomas 1956
- 7 Godtfredsen E & Lederman M Ophthalmological Signs and Symptoms in Malignant Nasopharyngeal Tumours Acta Neurol Scandinav 41 43 51 1965
- 8 Hestenbaum A Clinical Methods of Neuro ophthalmologic Examination Grune and Stratton N Y 1946
- 9 Lyle Donald J Divergence Insufficiency Arch Ophth 52 858 863 1954
- 10 Moller H U Personal Communication 1952
- 11 Scober R G & Green E L A Center for Ocular Divergence does it exist? Am J Ophth 29 422 434 1946
- 12 Walsh Frank B Clinical Neuro ophthalmology 2nd Edition 257 1957
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divided by blunt dissection and a tunnel is made with a finger in the loose tissue in front of the trachea into the mediastinum. It is usually easy to expose the trachea down to the bifurcation. The area is palpated, enlarged lymph nodes are usually readily palpable. The mediastinoscope is introduced (Fig 1) and via the scope the mediastinal tissue especially the lymph nodes may be dissected and biopsied. Histological examination has been carried out on the biopsy material together with examination for TB by guinea pig culture.

Material

The material is partly selected inasmuch as all our patients are referred to the department from practising ophthalmologists who themselves have treated the slight cases. Prior to the commencement of the study however we had asked that as many cases of uveitis as possible should be referred to the department.

Mediastinoscopy has not been carried out on 8 children below the age of 10 years and not on 7 patients above 70 years of age. Neither has it been carried out on 13 patients where the etiology was known on admission (Table 4). Finally it was not carried out on a further 3 patients by mistake.

There have been 108 cases of endogenous uveitis in the whole period, the 77 have been subjected to mediastinoscopy.

No lymph nodes were found in 3 cases during the attempt at mediastinal

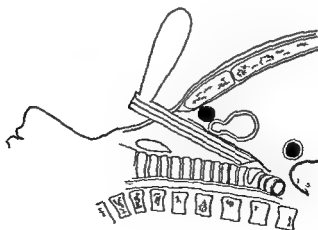


Fig 1

Schematic lateral view of mediastinoscope introduced in the correct plane beneath the pretracheal fascia.

Table 1
The frequency of sarcoidosis in surveys of uveitis in the literature as from 1950

Author	Year	Type of material	Total Patients	Number of sarcoidosis cases
Bjorkenheim ¹	1952		150	0
Vesterdal ²	1952	Endogenous uveitis	350	23
Woods et al. ³	1954	Chorioretinitis	301	12
Alvaro ⁴	1954		175	0
Bennett ⁵	1955	Primary uveitis	332	7
Stanworth et al. ⁶	1957	Endogenous uveitis	197	2 + 1 doubtful
Perkins ⁷	1961	Generalized uveitis	1718	55
Woods et al. ⁸	1961	Endogenous uveitis	123	19
Bergaust ⁹	1962		255	1
Giles ¹⁰	1963	Anterior uveitis in children under 16 years of age	16	9
Leira ¹¹	1965	Endogenous nonpurulent	420	1
Bergaust ¹²	1966	Patients of more than 50 years of age	121	1
Haut ¹³	1966	Endogenous 718 exogenous 132	850	7 + 4 doubtful
Hemmes ¹⁴	1968	Acute anterior uveitis	386	not stated

procedure has proved to be safe and of great clinical importance in various intrathoracic conditions e.g. bronchogenic carcinoma and sarcoidosis

The method has since in many centers become a routine examination inasmuch as it gives more positive findings than biopsy carried out according to the method of Daniels (16 17 18) or with biopsy of other organs (18) in patients suspected for sarcoidosis

Since 1964 we have carried out mediastinoscopy with lymph node biopsy from the superior mediastinum in patients with endogenous uveitis where we have no known etiology in order to find out whether the frequency of sarcoid iritis in unselected cases is larger than found until the present

Method

Mediastinoscopy with lymph node biopsy is carried out under general anaesthesia. The anterior wall of the trachea is freed throughout a 3-4 cm long transverse incision at the level of the suprasternal notch. The pretracheal tissue is

Table 9
Distribution of 108 cases of endogenous uveitis according to type

Diagnosis	- Mediastinoscopy	+ Mediastinoscopy - Sarcoidosis	+ Mediastinoscopy + Sarcoidosis	Total
Uveitis chron bilat	10	24	10	44
Uveitis acute bilat	3	5	4	12
Uveitis chron unilat	10	14	0	24
Uveitis acute unilat	8	90	0	28
Total	31	63	14	108

biopsy. In these 3 patients the histological diagnosis were respectively thymus tissue, thyroid tissue and fat tissue.

Complications

There have only been a few complications with the procedure in our material. One patient had postoperatively a temporary paralysis of the left recurrent nerve. In one patient there was haemorrhage from a small vein which however ceased on tamponade. In another a slight pneumothorax of no great importance occurred.

Results

Of the 77 patients that had been subjected to mediastinoscopy a histological picture compatible with sarcoidosis was found by histological examination in 14. I.e. 13 per cent of the whole series, 18.2 per cent of those who were subjected to mediastinoscopy, and 21.2 per cent of all the bilateral cases.

Table 2 and 3 show the distribution of the forms of uveitis in the material. It must however be mentioned that in 12 patients ophthalmoscopy was not possible either owing to a small synechial bound pupil or owing to complicated cataract. These patients are classified as panuveitis. All the patients with sarcoidosis could be subjected to ophthalmoscopy. In the 63 patients who had been subjected to mediastinoscopy without sarcoidosis being found the etiology was only discovered in 4. One was a patient where TB was found on cultivation from the biopsy material. One had toxoplasmosis with increasing titer with complement fixation test and dye test, one had temporal arteritis (Horton) verified by biopsy and one Mb. Reiter. In all the etiology was thus found in 31 patients (Table 4) which corresponds to 28.7 per cent of the whole material.

The Sarcoidosis Group

The 14 patients where the histological examination showed by typical epithelioid cell granuloma compatible with the diagnosis sarcoidosis were distributed with regard to age between 15 and 70 years. 8 of the patients were more than 50 years of age. There were 8 women and 6 men. As can be seen from table 2 all had bilateral uveitis.

The 4 patients classified as acute were admitted 10-14 days after the occurrence of the first symptoms and were healthy after approximately one month.

Table 2
Distribution of 108 cases of endogenous uveitis according to type

Table 2 Distribution of 103 cases of endogenous uveitis according to type				
Diagnosis	— Mediasinoscopy	+ Mediasinoscopy		Total
		— Sarcoidosis	+ Sarcoidosis	
Uveitis chron bilat	10	24	10	44
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Table 3
 Etiological factors in 103 patients with endogenous uveitis

— Mediastinoscopy	Morbus Bechterew	2
	Ulcerous Colitis	1
	Rheumatic Fever	1
	Influenza C.	1
	keratoiritis	1
	Lucs Cong (active)	1
	Ophthalmia Sympatica	1
	Rheumatoid Arthritis	1
	Morbus Still	2
	Varicella	1
	Ophthalmic Zoster	1
+ Mediastinoscopy	Temporal Arteritis (Horton)	1
	Morbus Reiter	1
	Toxoplasmosis	1
	Tuberculosis	1
	Sarcoidosis	14
Total		31

None of these have suffered from recurrence since. The period of observation is more than two years. All 4 were men between 30 and 50 years of age.

All the 10 classified as chronic had symptoms of more than 1 month's duration prior to admission and the majority had had previous attacks of uveitis. All have since been controlled for more than 11 months because of continuous or recurrent inflammation.

One patient had had recurrent uveitis for more than 20 years and had been admitted to various ophthalmological departments without the etiology having previously been found.

All of the patients had, similar to those without sarcoidosis, had topical steroid treatment from the practising ophthalmologist for a shorter or longer period prior to admission. A few had previously received systemic steroid treatment in smaller doses. The clinical ophthalmological picture might have been affected by this treatment.

We have not during the study had the impression that the group with sarcoidosis showed any characteristics compared with the patients not suffering from this disease.

Mutton fat, K, P were equally distributed between the two groups (in ap

Table 3
Distribution of 108 patients with endogenous uveitis according to localization

Diagnosis	— Mediastinoscopy	+ Mediastinoscopy — Sarcoidosis	+ Mediastinoscopy + Sarcoidosis	Total
Uveitis ant	9	15	1	25
Uveitis post	3	3	0	6
Panuveitis	19	45	13	77
Total	31	63	14	108

Symptoms from other Organs

Only a few of the patients had symptoms from other organs 3 of the patients had slight uncharacteristic symptoms of the joints

One patient was primarily admitted to the neurosurgical department for observation for an intracranial tumour owing to intracranial calcification around the sella and impaired vision Daniels biopsy had previously been performed on this patient owing to radiologically demonstrated enlarged hilar lymph nodes but this had been negative

One patient had Heerfordt's syndrome on admission

X ray examination of the lungs initially showed enlargement of the mediastinal lymph nodes in 7 patients In an additional 2 patients hilar changes were found by subsequent tomography No radiological changes of the thorax were found in the remaining 5 patients

None of the patients with demonstrable involvements of the mediastinal lymph nodes had had respiratory tract symptoms

Laboratory Tests

7 of the patients had a moderate increased sedimentation rate (17-44 mm/H) Of these 2 had a slightly increased Alpha serum globulin whilst one with a normal sedimentation rate also had the same increase

The Mantoux test was positive in 5 patients

Serum calcium was normal in all the patients

We have not used Arveim's skin test as all the patients were put onto systemic steroid treatment immediately after the mediastinoscopy had been carried out (19)

Treatment

All the patients were treated with corticosteroids both topically and systemically

We have not seen steroid induced increase in the intraocular pressure neither in the group with sarcoidosis nor the others

Comments

We consider that Carlen's introduction of mediastinoscopy with lymph node biopsy has made it possible for the ophthalmologist together with the endoscopist to find nearly all cases with uveitis caused by sarcoidosis

proximately 50 per cent) and were mainly seen in patients who had only been on steroid treatment for a short period prior to admission

Nodules of the iris were seen in 2 of the 14 sarcoidosis patients and in 6 of the remainder

Neither have we had any definite impression of a difference between the sarcoid- and the non sarcoid group following ophthalmoscopy and three mirror prism examination We have seen dilated veins periphlebitis perivenous nodules exudations and haemorrhages in both groups Similarly we have seen vitreous opacities, particularly "snowballs" in the periphery in both groups

We have counted the patients with iris nodules perivenous nodules and/or snowballs in the bilateral cases in both groups after the study had been finished and a clear difference could then be seen (table 5)

Typical candle wax exudates have only been seen in one patient who had sarcoidosis

None of the patients with sarcoidosis had conjunctival or scleral involvement Neither has keratoconjunctivitis sicca been seen

10 of the patients were admitted during the first attack This has in all probability contributed to the fact that the ophthalmological clinical picture in this group has been less distinct and with only few complications

Two of the sarcoid group have developed secondary glaucoma which could be regulated by epinephrine bitartrate

The patient who had suffered from recurrent uveitis for more than 20 years has now severely impaired visual acuity (3/60 on the best eye) partly owing to complicated cataract but especially owing to severe vitreous opacities

One man of 55 years was admitted after only having slight symptoms of uveitis for 14 days Despite intensive systemic steroid treatment he developed severe bilateral panuveitis retinal detachment in one eye with severe vitreous haemorrhages After a two years period of observation and systemic steroid treatment he still suffers from uveitis with recurrent attacks

Table 5

The presence of iris infiltrations snowballs and/or previous nodules in patients with acute or chronic bilateral uveitis (66 cases)

	Positive findings	Total number	%
Patients with sarcoidosis	8	14	57.1
Patients without sarcoidosis	7	42	21.4

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Patients with sarcoidosis	8	14	57.1
Patients without sarcoidosis	9	42	21.4

Symptoms from other Organs

Only a few of the patients had symptoms from other organs 3 of the patients had slight uncharacteristic symptoms of the joints

One patient was primarily admitted to the neurosurgical department for observation for an intracranial tumour owing to intracranial calcification around the sella and impaired vision Daniels biopsy had previously been performed on this patient owing to radiologically demonstrated enlarged hilar lymph nodes but this had been negative

One patient had Heerfordt's syndrome on admission

X ray examination of the lungs initially showed enlargement of the mediastinal lymph nodes in 7 patients In an additional 2 patients hilar changes were found by subsequent tomography No radiological changes of the thorax were found in the remaining 5 patients

None of the patients with demonstrable involvements of the mediastinal lymph nodes had had respiratory tract symptoms

Laboratory Tests

7 of the patients had a moderate increased sedimentation rate (17-44 mm/H) Of these 2 had a slightly increased Alpha serum globulin whilst one with a normal sedimentation rate also had the same increase

The Mantoux test was positive in 5 patients

Serum calcium was normal in all the patients

We have not used Kveim's skin test as all the patients were put onto systemic steroid treatment immediately after the mediastinoscopy had been carried out. (19)

Treatment

All the patients were treated with corticosteroids both topically and systemically

We have not seen steroid induced increase in the intraocular pressure neither in the group with sarcoidosis nor the others

Comments

We consider that Carlens' introduction of mediastinoscopy with lymph node biopsy has made it possible for the ophthalmologist together with the endoscopist to find nearly all cases with uveitis caused by sarcoidosis

proximately 50 per cent) and were mainly seen in patients who had only been on steroid treatment for a short period prior to admission

Nodules of the iris were seen in 2 of the 14 sarcoidosis patients and in 6 of the remainder

Neither have we had any definite impression of a difference between the sarcoid and the non sarcoid group following ophthalmoscopy and three mirror prism examination We have seen dilated veins periphlebitis perivenous nodules exudations and haemorrhages in both groups Similarly we have seen vitreous opacities particularly "snowballs", in the periphery in both groups

We have counted the patients with iris nodules perivenous nodules and/or snowballs in the bilateral cases in both groups after the study had been finished, and a clear difference could then be seen (table 5)

Typical candle wax exudates have only been seen in one patient who had sarcoidosis

None of the patients with sarcoidosis had conjunctival or scleral involvement Neither has keratoconjunctivitis sicca been seen

10 of the patients were admitted during the first attack This has in all probability contributed to the fact that the ophthalmological clinical picture in this group has been less distinct and with only few complications

Two of the sarcoid group have developed secondary glaucoma which could be regulated by epinephrine bitartrate

The patient who had suffered from recurrent uveitis for more than 20 years, has now severely impaired visual acuity (3/60 on the best eye) partly owing to complicated cataract but especially owing to severe vitreous opacities

One man of 55 years was admitted after only having slight symptoms of uveitis for 14 days Despite intensive systemic steroid treatment he developed severe bilateral panuveitis retinal detachment in one eye with severe vitreous haemorrhages After a two years period of observation and systemic steroid treatment he still suffers from uveitis with recurrent attacks

Table 5

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Comments

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The examination is not difficult to perform and is rather harmless with only a few and slight complications

In a series of 2500 cases from Sweden and Denmark (21) very few complications occurred 3 cases had recurrent nerve paralysis One had rupture of the bronchus resulting from biopsy of a carcinoma Slight haemorrhage can also occur however, this can be easily stopped by tamponade Pneumothorax can also develop

The procedure should be carried out by an experienced endoscopist working in cooperation with a thoracic center

There are only a few contra indications

The procedure can be difficult to carry out on smaller children owing to the lack of space It should not be carried out where a prior diagnosis exists and neither should it be done where other sites of the affection are more readily available and from which it is easier to obtain biopsy material as for example with palpable lymph nodes Neither should the procedure be carried out in patients where there is doubt as to whether or not they are able to stand general anaesthesia (18)

The advantages with the method are that it is possible to obtain an earlier and more certain diagnosis than by Daniels biopsy and in addition the procedure is more safe to perform (18)

The certainty of the diagnosis is as great as it is possible to obtain at present time namely the histological examination

A diagnosis of sarcoidosis can be obtained only by a study of the patient's case as a whole the history and the results of clinical radiographical bacteriological and laboratory investigations Confirmative histological evidence is desirable and should be sought whenever possible (18)

Pathologically the typical lesion is the so called epithelioid cell granuloma which independently of the location presents the same histological picture The granuloma which is characteristic and constitutes a necessary basis for a definite diagnosis consists of clusters of epithelioid cells surrounded by a narrow rim of lymphocytes Giant cells of both the Langhans and foreign body types are frequently present The histological appearance is similar to that of tuberculosis but there is no central necrosis and tubercle bacilli are absent (Fig 2)

The histological appearance of non caseating epithelioid cell granuloma is most often due to sarcoidosis These histological features however are also common to a large group of granulomatous infectious diseases including tuberculosis leprosy syphilis and others Therefore the histopathological reaction must always be interpreted in conjunction with the clinical features of the specific case

In relation to this it should be noted that one of our patients with bilateral uveitis had sarcoidosis like epithelioid cell granuloma in the histological sec



Fig 2

Microscopic section of mediastinal lymph node showing characteristic histological pattern of epithelioid cell granuloma containing multinucleated cells no evidence of necrosis (Hematoxylin and eosin $\times 100$)

tion and normal conditions in the chest radiography Cultivation from the lymph node biopsy demonstrated however growth of TB bacilli without the patient showing other signs of TB thus gastric lavage showed no growth of TB bacilli

In three other patients with bilateral uveitis epithelioid cells suggestive of sarcoidosis were found during histological examination However these cells did not show the typical granuloma arrangement and therefore these 3 patients were not included in the survey

It can be seen from table 1 that the frequency of sarcoidosis varies enormously as the etiological factor of uveitis None of the investigators however have been particularly interested in obtaining the diagnosis sarcoidosis The figures cannot be compared without reservation particularly owing to the different methods of examination used in order to obtain the diagnosis sarcoidosis A negative biopsy according to the method of Daniels or the absence of hilar lymphadenopathy during x ray examination does not exclude by any means the sarcoidosis as the cause of a uveitis

It is interesting that 5 of our 14 patients with sarcoidosis had normal chest

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lary lymph nodes and among these microscopy demonstrated in 14 cases giant cell granuloma as an expression of sarcoidosis

No serious complications followed the mediastinoscopy which was performed under general anaesthesia by the chest surgeons

X ray of the chest showed definite normal conditions in 5 of the patients in whom mediastinoscopy with biopsy demonstrated sarcoidosis

References

- 1 Björkenheim B Aetiology of Uveitis *Finska Läkare Samfundets Handl* 9: 146-153 1957
- 2 Vesterdal H Indocyclitis Clinical Studies on Aetiology Pathogenesis and Therapy with ACTH and Cortisone København Nyt Nordisk Forlag Arnold Busck
- 3 Woods A C et al A Study of the Role of Toxoplasmosis in Adult Chorioretinitis *Amer J Ophthalmol* 37 163 177 1954
- 4 Alvarez M E The Etiology of Uveitis *Ophthalmologica* 127 85 93 1954
- 5 Bennett C Uveitis A Clinical and Statistical Survey *Brit J Ophthalmol* 39 707 742 1955
- 6 Stanworth A & McIntyre H Aetiology of Uveitis *Brit J Ophthalmol* 41 380 420 1957
- 7 Perkins E S Uveitis and Toxoplasmosis London Churchill 1961
- 8 Woods A C & Abrahams I W Uveitis Survey *Amer J Ophthalmol* 51 761 780 1961
- 9 Bergaust B Uveitis as Seen in Material from a Hospital in the Arctic Circle (Tromsø) *Acta Ophthalmol* 30 443 452 1962
- 10 Giles C L Anterior Uveitis in Children. *Arch Ophthalmol* 0 7:9 785 1963
- 11 Leira H Studies on Causal Relations in Endogenous Non Purulent Ocular Inflammations København Munksgaard 1965
- 12 Bergaust B The Etiology of Uveitis in the Ages Geriatrics 21 145 154 1966
- 13 Haut J Etiologic Classification of Uveitis in 850 Cases *Arch Ophthalmol* 66 691 694 1966
- 14 Hemmes G D Acute Anterior Uveitis of Unknown Origin and its Connection with Herpes Simplex *Ophthalmologica* 15 300 307 1968
- 15 Carlens H Mediastinoscopy A Method for Inspection and Tissue Biopsy in the Superior Mediastinum *Dis Chest* 36 343 352 1959
- 16 Nielsen E Graven & Olsen H Mediastinoscopy An Analysis of 223 Cases *Dan Med Bull* 13 195 197 1966
- 17 Lofgren S & Snellman R Principles and Procedures for Obtaining Biopsies in Sarcoidosis *Acta Med Scand Suppl* 470 225 227 1964
- 18 Jepsen O Mediastinoscopy Bioptic Mediastinal Exploration on the Method of Carlens København Munksgaard 1966
- 19 Scadding J C Sarcoidosis London Fyre & Spottis Woods 1967
- 19 Kaufman H E The Uvea *Arch Ophthalmol* 75 407 414 1966
- 19 Carlens E & Jepsen O Mediastinoscopy *Otolaryngologic Clinics of North America* 171 195 1963
- 19 Jepsen O Personal communication 1963

radiographs *Jepsen* (22) reports that he in a series of 81 patients with sarcoidosis found that 9 of the patients had normal findings with radiological examination of the thorax similar to the cases referred to here

The frequency of sarcoidosis stated in literature varies considerably (23)

In Denmark 5 new cases per 100 000 inhabitants are reported annually. It is considered that approximately 80 per cent of the cases are reported (24). Our department serves a population of approximately 250 000. Compared with the above it would mean that there during a 4 year period, should be at least 67 new cases of sarcoidosis. *James* (25) has found that approximately 20 per cent of the cases of sarcoidosis have uveitis which again would mean that we in the period under study should have found approximately 12-13. This theoretical figure corresponds well to our result. The fact that *Scadding* (19) finds that approximately 10 per cent of all the cases of sarcoidosis commence with uveitis, also corresponds well to our results. Our series is small but it is remarkable that so few patients have had general symptoms. Similarly it has also been remarkable that all the cases with a few exceptions have only presented vague symptoms. None of the patients with sarcoidosis had such severe and characteristic findings in the anterior part of the eye as described by *Woods* (26) but this may be due to early steroid treatment which as stated by *James* (21), results in a striking improvement in patients who are treated within one or two years of the onset of the disease.

Based upon the cases we have seen we must agree with *Wilmer* (28) that no findings are pathognomonic for uveitis based on sarcoidosis. Characteristic changes occur more frequently in sarcoidosis patients but none of these changes are pathognomonic for this disease.

In contrast to *James* (25) who in his material mainly found anterior uveitis we found only one patient with anterior uveitis whilst the remaining 13 were panuveitis and we have not been able in our small sarcoidosis material to demonstrate two quite different syndromes as stated by him.

This study will be continued partly for scientific reasons partly also to see whether the early institution of steroid treatment with sarcoidosis will prevent severe reduction in visual acuity (29) and whether it can prevent other manifestations.

Abstracts

In a material of 108 patients with endogenous uveitis sarcoidosis was found to be the etiological factor in 13% of the whole material and in more than 20% of the bilateral cases.

In 77 of these patients mediastinoscopy was performed with biopsy of the hi

lary lymph nodes and among these microscopy demonstrated in 14 cases giant cell granuloma as an expression of sarcoidosis

No serious complications followed the mediastinoscopy which was performed under general anaesthesia by the chest surgeons

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References

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- 3 Woods A C et al A Study of the Role of Toxoplasmosis in Adult Chorioretinitis *Amer J Ophthal* 37 163 177 1954
- 4 Altaro V E The Etiology of Uveitis *Ophthalmologica* 127 85 93 1954
- 5 Bennett G Uveitis A Clinical and Statistical Survey *Brit J Ophthal* 39 727 749 1955
- 6 Stanworth A & McIntyre H Aetiology of Uveitis *Brit J Ophthal* 41 385 470 1957
- 7 Perkins H S Uveitis and Toxoplasmosis London Churchill 1961
- 8 Woods A C & Abrahams I W Uveitis Survey *Amer J Ophthal* 51 161 780 1961
- 9 Bergaust B Uveitis as Seen in Material from a Hospital in the Arctic Circle (Tromsø) *Acta Ophthal* 30 443 452 1962
- 10 Giles C L Anterior Uveitis in Children *Arch Ophthal* 10 119 180 1963
- 11 Leira H Studies on Causal Relations in Endogenous Non Purulent Ocular Inflammations København Munksgård 1965
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- 13 Haut J Etiologic Classification of Uveitis in 850 Cases *Arch Ophthal* 26 691 694 1966
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- 17 Lofgren S & Snellman B Principles and Procedures for Obtaining Biopsies in Sarcoidosis *Acta Med Scand Suppl* 402 925 927 1964
- 18 Jepsen O Mediastinoscopy Bioptic Mediastinal Exploration on the Method of Carlens København Munksgård 1966
- 19 Scadding J G Sarcoidosis London. Eyre & Spottis Woods 1967
- 20 Kaufman H E The Uvea *Arch Ophthal* 75 407 434 1966
- 21 Carlens E & Jepsen O Mediastinoscopy *Otolaryngologic Clinica of North America* 171 193 1969
- Jepsen O Letteral communication, 1969

- 23 *Bauer H & Lofgren S* International Study of Pulmonary Sarcoidosis in Mass Chest Radiography *Acta Med Scand Suppl* 425 103 105 1964
- 24 *Horuit- O et al* Epidemiology of Sarcoidosis in Denmark. *Dan Med Bull* 14 178 182 1967
- 25 *James D G et al* Ocular Sarcoidosis *Brit J Ophthal* 48 461 470 1964
- 26 *Woods A C* Endogenous Inflammations of the Uveal Tract Baltimore Williams & Wilkins 1961
- 27 *James D G* Treatment of Sarcoidosis *The Lancet* (Sept. 9) 526 528 1967
- 28 *Witmer R* Klinik der Uveitis Labordiagnostik *Ophthalmologica* 149 390 404 1965
- 29 *Beck A* Chronic Iridocyclitis An Analysis of the Occupational Prognosis in a Series of Patients from the Royal Institute for the Blind *Acta Ophthal* 39 963 963 1961

JUDICIA DE NOVIS LIBRIS

Arnall Pat & Richard E Hooter Protection of Vision in Children Springfield. Charles C. Thomas 1969 Pp 177 Price 10 \$

This book is not written for eye specialists but for pediatricians family and school physicians teachers and parents. In this respect it presents valuable information about the conditions and affections commonly inducing visual defects. The major project should be a visual or better eye screening in pre school age or as early as possible. An interesting eye screening is the simple photographic recording of the eyes of infants with a portable camera. The photographs are reviewed by an ophthalmologist in much the same way X ray films are read by radiologists. The problems of oxygen for pre matures and in respiratory distress are dealt with and so are genetic counseling for eye disorders protection against and management of eye injuries reading problems and optical aids.

P Brandstrup

Biblioteca degli Annali di Ottalmologia e Clinica Oculistica Volume I Scritti in onore del Prof Luigi Maggiore Parma Maccani 1968 Pp 403

An imposing volume honouring emeritus professor Luigi Maggiore of the university eye department in Genova Italy 41 excellent contributions

P Brandstrup

Kittel Viktor Therapeutische Empfehlungen zur Behandlung von Augenkrankheiten. 2nd ed. Leipzig VEB Georg Thieme 1969 118 pages (Abhandlungen Augenheilkunde Vol 31) Price M 14.90

This little book, written by Professor Kittel of the Eye Clinic, Berlin, D.D.R. is addressed mainly to the younger ophthalmologists. A number of the therapeutic principles agree with those in use in Denmark.

In panophthalmitis irrigation of the anterior chamber with antibiotics (penicillin, chloramphenicol, tetracyclines, erythromycin) is used.

The amino acid antagonist Almasid (fluorophenylalanine) is mentioned as a possible iridocyclolytic agent in the treatment of viral disease.

Among older remedies injections of dionine and milk are still used.

Temporal arteritis is treated by bilateral resection of the temporal arteries instead of immediate steroid medication.

Subconjunctival implantation of placental tissue in retinitis pigmentosa has been tried but without definite objective improvement.

The indications for systemic steroid therapy and for systemic vascular dilatation appear to me to be too wide.

In recurrent corneal erosion a local anaesthetic even cocaine ointment, is recommended although in our opinion this is contra indicated.

Drexler's flame sterilization of tonometers is rightly emphasized in preference to cleaning the tonometer footplate with ether or with hydroxyethoxycyanate.

It is interesting to observe the difference between East German and Scandinavian

- 23 *Bauer H & Lofgren S* International Study of Pulmonary Sarcoidosis in Mass Chest Radiography *Acta Med Scand Suppl 425* 103 105 1964
- 24 *Horwitz O et al* Epidemiology of Sarcoidosis in Denmark *Dan Med Bull 14* 178 182 1967
- 25 *James D G et al* Ocular Sarcoidosis *Brit J Ophthal 48* 461 470 1964
- 26 *Woods A C* Endogenous Inflammations of the Uveal Tract Baltimore Williams & Wilkins 1961
- 27 *James D G* Treatment of Sarcoidosis *The Lancet* (Sept 9) 576 578 1967
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about the possibilities and advantages by this differentiated examination of the normal ocular fundus and in common and more rare affections. The documentation is accompanied by many instructive coloured drawings which illustrate the varied and interesting configurations of the fundal details when observed in the differently coloured light.

P. Brændstrup

tradition but apart from that the book is probably not of major interest to Scandinavian ophthalmologists

M S Norr.

Walsh Frank B and Hoyt W Fletcher Clinical Neuro Ophthalmology 3rd edition Vol I II & III 2763 pages The Williams & Wilkins Co Baltimore, 1969 Price \$ 120 00

Walsh's Neuro Ophthalmology has always been a voluminous book but this 3rd edition is larger than any before it having almost 3000 double columned pages. This edition also has a much larger number of illustrations than the earlier ones.

The first edition appeared in 1947 and was reprinted in 1948 and 1952. Then, the second edition appeared in 1957 reprinted in 1961. The third edition is no reprint or either a revised edition but has been almost completely rewritten.

Of course it is a matter of judgment how much neurology and how much ophthalmology is to be included in a Neuro Ophthalmology. The authors have included a great deal and that is a good thing because then we can still resort to Walsh when faced with puzzling cases in practice.

Another good thing is the large number of case reports scattered in the text to illustrate so admirably and supplement the description of many of the disease conditions.

The first volume in its first four chapters provides basic information pertaining to the functional anatomy of the visual oculomotor sensory and autonomic nervous systems. The fifth chapter concerns the diagnosis of changes in the optic disc. Chapter 6 deals with congenital anomalies and Chapter 7 with hereditary and degenerative diseases.

In Vol II metabolic and toxic diseases muscular disorders infections parasitic invasions and vascular lesions are described.

The contents of Vol III are Orbital ocular and intracranial tumours traumas ocular signs in neurasthenia hysteria and malingering. This is followed by an account of neurotoxic substances affecting the visual and ocular motor systems.

In such a book which is intended to serve as a manual it is of course of the utmost importance that the subject indices be as exhaustive and accurate as they are. It greatly facilitates the survey that a complete subject index for all 3 volumes is printed at the end of each volume. A special index of drugs and toxic substances is also given.

The references from previous editions have been supplemented by numerous modern ones.

The previous editions of Walsh Neuro Ophthalmology were good too but this 3rd edition is increased and renewed. Walsh has kept up to date and is still at the top as an extremely useful source of clinical ophthalmoneurological information.

Holger Ehlers

А М Водовозов «Офтальмохромоскопия» A M Vodovozov Ophthalmochromoscopy Moscow Meditsina 1969 Pp 168 Figg 217 Price 3p 03k

This atlas written in Russian represents an introduction in ophthalmoscopy with lights of different spectral composition red yellow blue yellowish green and purple ophthalmochromoscopy. After a description of the special technique follows information

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ZUR FRAGE DES GLEICHZEITIGEN VORKOMMENS VON GLAUKOM UND COCHLEO VESTIBULAREN STÖRUNGEN

VON

H. P. VICK und U. VICK

Seit von Hansen (1880) und von Rampoldi (1889) auf die Beziehungen zwischen Menierescher Erkrankung (Hansen) bzw. Schwerhörigkeit (Rampoldi) und Glaukom hingewiesen wurde, haben sich zahlreiche Untersucher mit dem Vergleich der Druckverhältnisse im Auge und Innenohr befasst. Dass bis heute noch nicht zu einer Beantwortung dieser Frage gekommen ist, deutet auf die Schwierigkeiten dieses Problems hin.

Relativ häufig beschrieben ist das synchrone Auftreten von akuten intraokularen Drucksteigerungen bei der Meniereschen Erkrankung; umgekehrt kann es beim akuten Glaukom zu Meniereschen Symptomen kommen, so dass gelegentlich die Bezeichnung „extraokulares Glaukomsymptom“ (Tille) gebraucht wurde.

Die anatomischen Analogien von Auge und Innenohr, insbesondere das Vorhandensein eines Flüssigkeitskörpers in beiden Sinnesorganen, lassen an gemeinsame pathologische Momente bei der hydrodynamischen Dystonie, als die sowohl das Glaukom wie auch die Menieresche Erkrankung aufgefasst werden können, denken (Sokolowski, Godfredsen, Mc Grath, Magdalena Castaneira, Ten Doesschate *et al.*).

Nicht nur beim akuten Glaukom, sondern auch bei chronischen Glaukomformen soll es nach Ansicht zahlreicher Autoren signifikant häufig zur Mitbeteiligung des stato-akustischen Organes kommen. Insbesondere wird immer wie-

Eingegangen am 1. Juni 1969

*5th Vienna Seminar on Clinical Echoophthalmography
(training program for beginners and advanced students)*

Date 11 15 May 1980

Place II Ophthalmology Service (Head Prof Dr J Boeck) University of Vienna
Medical School Alserstrasse 4 1090 Vienna Austria

Languages English French German

Subjects

- 1 Basics - physics and technology of ultrasound
- 2 A simple and quick method for testing system performance
- 3 Optimum system settings for clinical work
- 4 Examination technique (echography of the eye and orbit)
- 5 Ultrasonic (differential) diagnosis in diseases of the eye retinal and choroid detachment choroid sarcoma metastatic carcinoma benign tumors pseudotumors retinoblastoma retrolental fibroplasia hemorrhages and other opacities of the vitreous foreign bodies etc
- 6 Ultrasonic (differential) diagnosis in diseases of the orbit tumors pseudotumors traumatic changes endocrine exophthalmos foreign bodies etc
- 7 Non traumatic tissue differentiation by ultrasound
- 8 Ultrasonic oculometry
- 9 Kretztechnik's new standardized diagnostic system (series 7200) for use in ophthalmology and tissue differentiation

For inquiries and registration

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Alserstrasse 4 1090 Vienna Austria

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Frühsymptom des Glaukoms sehen. So soll bei Glaukomanfallsbereitschaft der Lautheitsausgleich auftreten und in der normotonen Periode wieder verschwinden. Diese für die Glaukomdiagnostik sehr hoffnungsvoll klingenden Ergebnisse konnten jedoch von anderer Autoren nicht bestätigt werden und haben somit keinen Einzug in die Glaukomdiagnostik gefunden.

Pietruschka schliesst aus der audiometrischen Untersuchung von 120 Glaukompatienten (35 Glaucoma simplex 30 Glaucoma chronicum congestivum 20 akute Glaukome 10 Sekundärglaukome 3 Pseudoglaukome 3 Buphthalmus Patienten) dass besonders nach dem 50 Lebensjahr häufig eine über das altersgerechte Hören hinausgehende Innenohrschwerhörigkeit auftritt die sich aber nicht von der Presbykussis abtrennen lässt und Ausdruck der bei Glaukompatienten festgestellten Häufigkeit der Arteriosklerose sein konnte. Einen sicheren Zusammenhang zwischen Glaukom und Schwerhörigkeit sieht Pietruschka nicht insbesondere da sonst viel häufiger Beziehungen zwischen dem Ausmass der glaukomatösen Veränderungen am Auge und dem Grad der Schwerhörigkeit auffallen müssten. Auch waren bei seitendifferenten Augenbefunden entsprechende Audiogramme zu erwarten. Ebenso aussert sich Leydhecker zurückhaltend und betont dass auf Grund der vorliegenden Untersuchungen ein signifikantes Zusammentreffen von Glaukom und Hypakussis als nicht gesichert angesehen werden kann. Schroder gibt zu bedenken dass das chronische Glaukom vorwiegend in höheren Altersklassen vorkommt und dass man die Kombination Glaukom mit Schwerhörigkeit bei Hörverlust in den hohen Frequenzen zunächst einmal auf das Alter beziehen muss. Massimeo und Salonna heben hervor dass man cochleo vestibuläre Störungen bei Glaukomkranken nicht in jedem Fall in ursächlichem Zusammenhang sehen sollte. Die Autoren untersuchten 34 Glaukompatienten sie fanden in 21 Fällen eine Innenohrschwerhörigkeit im Bereich der hohen Frequenzen und zweimal eine Vestibulärstörung. Da es sich jedoch durchweg um Patienten im fortgeschrittenen Alter handelte und die gefundenen Audiogramme fast ausnahmslos typischen Bildern der Altersschwerhörigkeit entsprechen warnen die Autoren vor zu weitgehenden Schlüssen.

So gehen die bisherigen Meinungen zum Problem Glaukom und Schwerhörigkeit von absoluter Bejahung über zurückhaltende Auffassungen bis zur Ablehnung eines Zusammenhanges weit auseinander.

Untersuchungsmethode

115 in der Universitäts Augenklinik Rostock stationär behandelte Glaukompatienten wurden in der Universitäts Hals Nasen und Ohrenklinik Rostock einer eingehenden Untersuchung des Hör- und Gleichgewichtsorganes unterzogen.

der auf den Zusammenhang zwischen Glaukom und Innenohrschwerhörigkeit hingewiesen Lampé und Mitautoren untersuchten 33 Patienten mit primärem Glaukom und fanden bei 30 eine »Schwerhörigkeit nervalen Ursprungs« Curlo sah unter 15 Patienten mit Glaucoma simplex 5 mit einer hochgradigen Schwerhörigkeit die im Innenohr oder weiter zentral lokalisiert war Als Ursache nimmt der Autor gefassneurotische Störungen vermutlich durch Schädigung des Sympathicus an Beretta et al kommen nach Untersuchung von 42 Patienten mit Glaucoma chronicum und 2 Fällen von akutem Glaukom zu dem Schluss dass insbesondere beim chronischen Glaukom ein pathogenetischer Zusammenhang zwischen Glaukom und Schwerhörigkeit sehr nahe liegt wobei gleichzeitige neurovegetative Störungen der Kapillardurchlässigkeit sowohl im Innenohr als auch in der Uvealmenbran des Auges ursächlich erwogen werden

Sokolowski registrierte bei 40 Glaukomkranken in 38% eine Hypakusis. Bietti und Porta konnten bei Glaukompatienten bei Flüssigkeitsbelastungsproben eine Parallelität zwischen der Zunahme des intraokularen Druckes und der audiometrisch nachweisbaren Hörminderung feststellen Bei Augengesunden blieb das Audiogramm bei Flüssigkeitsbelastungen unbeeinflusst (Bietti) Ten Doesschate audiometrierte 26 Glaukompatienten und kam zu dem Ergebnis dass denselben eine Perzeptionsschwerhörigkeit gemeinsam ist die in ihrem Ausmass Beziehungen zum intraokularen Druck weniger zur Einschränkung des Gesichtsfeldes aufweist Czaplicka und Mitarbeiter stellten bei 21 Untersuchten mit Glaucoma simplex in 66% eine Perzeptionsschwerhörigkeit fest Die Autoren sahen in dem hohen Prozentsatz den Beweis für einen ursächlichen Zusammenhang zwischen beiden Krankheiten Eine Abhängigkeit zwischen dem Grad der Augenerkrankung und dem Funktionsverlust des Innenohres war nicht erkennbar

Gartner gelangte durch das von ihm beobachtete gehäufte Auftreten von Innenohrschwerhörigkeit beim Pigmentglaukom zu der Auffassung dass in diesen Fällen möglicherweise ein Zusammenhang der Pigmentstörung im Auge mit einer entsprechenden Störung des Innenohrpigments vorliegt Bei 6 Patienten mit Pigmentglaukom hatte der Autor in 4 Fällen eine ungeklärte Innenohrschwerhörigkeit gefunden Diese Ansicht wurde Unterstützung finden durch die Beobachtung von Innenohrschwerhörigkeit bei sympathischer Ophthalmie Vogt Koyanagi - Syndrom und Haradascher Erkrankung Auch hier wurde auf eine komplexe Störung des Pigmentes hingewiesen (Hager Peters) Kramer et al nehmen auf Grund ihrer Untersuchungen an dass ein ursächlicher Zusammenhang zwischen Glaukom und Innenohrschwerhörigkeit besteht Von 124 Glaukompatienten wiesen 42 eine über das altersphysiologische Mass hinausgehende Perzeptionsschwerhörigkeit auf vorwiegend vom cochleo basalen Typ wie sie auch bei der Presbyakusis gefunden wird Chilaris et al wie auch Ferraris de Gaspare und Mitarbeiter gehen sogar so weit dass sie im Verhalten des charakteristischen Audiogramms und im Auftreten des Recruitmentphanomens ein

Tabelle II
Gegenüberstellung von Glaukomyt zu II rveru ogen der Glaukoupatienten

	Glaucoma simplex	Chron kong Glaukom	Akutes Glaukom	Irgent glaukom	Juveniles Glaukom	Buphthalmus	Summe
Nur mit Iren le	93	6	-	4	3	1	54
Altersgerechtes II rveru ogen	17	4	-	3	-	-	24
Innen Irschwerhorigkeit mit geklarter Ätiologie	1	9	1	-	-	-	19
Innen Irschwerhorigkeit unklarer Genese	15	1	1	-	1	-	18
	85	16	2	7	4	1	115

Tabelle I

Die 115 untersuchten Glaukompatienten liessen sich nach Glaukomtyp Geschlecht und Durchschnittsalter aufgliedern

Glaukomart	Anzahl	Geschlecht		Durchschnittsalter
		♂	♀	
Glaucoma simplex	85	33	47	53.4
Glaucoma chronicum congestivum	16	0	7	56.4
Akutes Glaukom	2		2	63.5
Pigmentglaukom	7	5	2	56.6
Juveniles Glaukom	4	4		27.8
Buphthalmus	1	1		12.0
Summe	115	57	58	47.8

Bei der Erhebung der Anamnese wurde besonders auf durchgemachte Infektionen und Intoxikationen chronische und akute Lärmtraumen sowie Stoffwechselerkrankungen Wirbelsäulenerkrankungen und Schädelunfälle geachtet. Nach der audiometrischen (Schwellenaudiogramm Geräuschaudiogramm nach Langenbeck) und röntgenologischen (nach Stenvers bzw. Pyramidenvergleichsaufnahmen) Untersuchung erfolgte die Prüfung des Vestibularorgans (Schwindelanamnese Prüfung des Lage und Lagerungsnystagmus sowie thermische Reizung).

Untersuchungsergebnisse

Die audiometrische Untersuchung ergab bei 54 (47.0 %) der 115 Patienten ein normales Hörvermögen mit einem Kurvenverlauf des Audiogramms für Luft- und Knochenleitung zwischen 0 und 10 dB. Von den verbleibenden 61 Patienten (53.0 %) zeigten 24 einen rein altersbedingten Gehörnachlass, wobei die diesbezügliche Bewertung nach den von Jatho und Heck angegebenen Hörkurven erfolgte.

37 Probanden wiesen also eine über das ihrem Alter entsprechende physiologische Mass hinausgehende Schwerhörigkeit auf. Von dieser Gruppe mussten jedoch bei kritischer Auswertung 19 Patienten abgesondert werden auf Grund langjähriger Lärmexposition akuter Lärmtraumen und Schädelverletzungen sowie Schalleitungsschwerhörigkeiten. Zu dieser Gruppe gehörten auch 3 Patienten mit einer kombinierten Schwerhörigkeit, bei denen man eine toxische Genese des Innenohrschadens annehmen musste.

Tabelle II
Gegenüberstellung von Glaukomtyp zum Horvermögen der Glaukomatischen

	Glaucoma simplex	Chron. long. Glaukom	Akutes Glaukom	Pigment glaukom	Juveniles Glaukom	Buphthalmus	Summe
Nur althorende	39	8	-	4	3	1	54
Altergerechtes Horvermögen	17	4	-	3	-	-	24
Innen- Irregularität mit geklarer Ätiologie	15	3	1	-	-	-	19
Innen- Irregularität mit unklarer Genese	15	1	1	-	1	-	18
	85	16	2	7	4	1	115

Es blieben 18 (15,8 %) Patienten mit einer über das altersphysiologische Mass hinausgehenden Innenohrschwerhörigkeit die auch bei sehr kritischer Bewertung der Anamnese und des objektiven Ohrbefundes zunächst atologisch nicht zu klären war. Bei diesen Probanden ist ein Zusammenhang zwischen dem Glaukom und der Innenohrschwerhörigkeit zu diskutieren. Einschränkend muss jedoch schon hier gesagt werden, dass es sich bei einem Teil der Fälle nur um gering über das altersphysiologische Mass hinausgehende Perzeptionsschwächen handelt.

Um die Lokalisation des Hörschadens im Labyrinth bei den 18 atologisch unklaren Hörminderungen näher zu bestimmen wurden die Audiogramme nach Langenbeck in vier Haupttypen eingeteilt. Dabei zeigte sich, dass in überwiegender Anzahl (13 von 18) der Kurventyp A (cochleo-basaler Typ) auftrat, wie er bevorzugt für die Altersdegeneration des Hörorgans typisch ist (Tab. III). Dieses Ergebnis unterstützt die von Pietruschka geäußerte Meinung, dass es auf Grund einer verstärkten Arteriosklerose bei Glaukompatienten zu einer über das Alter hinausgehenden Presbyakusis kommen kann.

Unter den 18 Patienten mit den atologisch unklaren Innenohrschwerhörigkeiten ergaben sich bei 8 Kranken seitendifferente Audiogramme, wobei jedoch nur einmal eine Übereinstimmung mit einem entsprechenden seitendifferenten Augenbefund bestand.

Bei der Gegenüberstellung der Audiogramme und der augenärztlichen Befunde konnte keine Abhängigkeit des Hörbefundes zur Glaukomdauer, zum Visus und Gesichtsfeldverfall sowie zum Grad der glaukomatösen Exkavation der Papillen gefunden werden. Ebenfalls ergaben sich keine Beziehungen zwischen der Höhe des intraokularen Druckes, der Weite des Kammerwinkels, der eingeschlagenen medikamentösen oder operativen Druckregulierung und dem Hörkurvenverlauf. So wurde z. B. bei beiden Patienten mit akutem Glaukom

Tabelle III

	Glaucoma simplex	Chron. kong. Glaukom	Akutes Glaukom	Juveniles Glaukom	Summe
A Corti Typ	■	1	1	1	3
C Corti Typ	1	—	—	—	1
A Corti/Nerv Typ	1	—	—	—	1
C Corti/Nerv Typ	1	—	—	—	1
A/C Typ	2	—	—	—	2
B/C Typ	1	—	—	—	1
	15	1	1	1	18

im Anfall ein Audiogramm am Krankenbett geschrieben und es zeigten sich nach erfolgter Drucksenkung (einmal medikamentös einmal operativ) bei einem Kontrollaudiogramm keinerlei Differenzen im Kurvenverlauf

Diese Ergebnisse decken sich mit den Aussagen von Pietruschka Kramer et al Czaplicka et al Lampe et al. und stehen im Gegensatz zu den Befunden von Tillé Ten Doesschate et al und Bietti c. s. die Zusammenhänge zwischen der Höhe des intraokularen Druckes bzw der Dauer des Glaukoms und dem Grad der Innenohrschwerhörigkeit sahen

Bei der Prüfung des Vestibularorgans fand sich unter den 115 Glaukompatienten nur in 2 Fällen eine Untererregbarkeit bei der kalorischen Reizung Ein Patient wies einen horizontalen mittelfrequenten mittellamplitudigen Spontan nystagmus auf und bei einem weiteren Patienten bestand eine einseitige Untererregbarkeit bei normaler Erregbarkeit des anderen Labyrinths 14 Untersuchte klagten bei der anamnestischen Befragung über Schwindel Bei allen Patienten ergab sich keine Korrelation zum Augen- und Hörbefund

Zusammenfassung

Um einen in der Literatur wiederholt beschriebenen Zusammenhang zwischen dem funktionellen und organischen Befund beim primären Glaukom und entsprechenden Hörstörungen am Innenohr nachzuprüfen wurden bei 115 Glaukomkranken eingehende Untersuchungen des Hör- und Gleichgewichtsorgans durchgeführt Auf Grund der mitgeteilten Untersuchungsergebnisse scheint kritische Zurückhaltung bei der Beurteilung des Zusammenhanges zwischen Glaukom und Innenohrschwerhörigkeit geboten

In untersuchen Beobachtungsgut steht den 18 Patienten mit einer ätiologisch unklaren Innenohrschwerhörigkeit eine Gruppe von 91 Glaukompatienten mit normalem bzw altersentsprechendem Hörvermögen oder eindeutig anamnestisch erklärbarer Schwerhörigkeit gegenüber

Ein gemeinsamer Faktor der beiden Erkrankungen in signifikanter Häufigkeit zu Grunde liegen konnte nicht aufgedeckt werden Bei der Auswertung der Geräuschaudiogramme nach Langenbeck fand sich überwiegend der Cochleo basale Typ (Typ A) der charakteristisch bei altersdegenerativen Prozessen häufiger vorkommt

Wenn die relativ geringe Anzahl von Schwerhörigkeiten unter unseren untersuchten Glaukompatienten in einem gewissen Widerspruch zu Ergebnissen anderer Untersucher steht so ist dies möglicherweise mit dem bewusst niedrig gehaltenen Durchschnittsalter unserer Probanden zu erklären

Zwischen dem Grad der glaukomatösen Veränderungen und den Hörkurven sowie den Vestibularisbefunden bestanden keine Beziehungen

Literatur

- Beretta L & E Cerabolini* Riv Oto neuro oftalm 32 662 677 (1957) ref Zbl ges Ophthalm Bd 74 (1958) S 266
- Bietti G B* Trans Ophthalm Soc U k 72 343 355 (1952) ref Zbl ges Ophthalm 59 373 (1953)
- Bietti G B & C F Porta* Oto rino laring ital 20 352 (1959) Zbl HNO 41 501 (1953)
- Chilaris G & A Cojas* J of Laryng 1961 Bd 75 S 501
- Ciurlo L* Arch ital otol 1937 Bd 49 497 518 ref Zbl ges Ophth 1938 Bd 40 H 5 S 307
- Czuplińska St & J Kuźniar* Otolaryng pol 20 449 453 (1966) ref Zbl HNO 93 495 (1967)
- Ferraris de Gaspare P F & G Maffei* Riv oto neuro oftalm 26 294 316 (1951) ref Zbl HNO 44 396 (1952)
- Gartner J* Ophthalmologica 147 S 393 408 (1964)
- Godtfredsen E* Bull soc franc ophthalm 63 295 (1950) ref Zbl ges Ophthalm 56 148 1951/52
- Mc Grath H* Amer J Ophth 35 241 245 (1952)
- Hager G* klin Mbl Augenhk 131 59 (1957)
- Hansen* Hdb d Physiologie der Sinnesorgane hrsg v Herrmann 1880 zit n. A Meyer zum Gottesberge Hdb HNO III/2 S 1662
- Jatho K & K H Heck* Zbl Laryng Rhinol 1959 Bd 38 S 12 88
- Kramer K, Frey H H & M Remsch* Klin Mbl Augenhk 151 51 (1967)
- Lampe J G H Tomits & F Csullog* klin Mbl Augenhk 143 542 (1963)
- Langenbeck B* Lehrbuch der prakt Audiometrie 3 Aufl G Thieme Stuttgart 1963
- Lejdzhecker W* Glaukom (Ein Handbuch) Springer Verlag (Berlin Göttingen Heidelberg) 1960 S 317 318
- Magdalena Castineira J* An Fac Med Santiago Compostela 1956 Bd 1 S 61 144 ref Zbl ges Ophth 1957 Bd 71 S 246
- Massimeo A & F Salonna* Riv oto neuro oftalm 1958 Bd 33 S 569 591 Zbl HNO 63 268 (1959)
- Peters A* klin Mbl Augenhk 506 433 (1912)
- Pietruschka G* klinische Untersuchungen zur Frage der Ätiologie des primären Glaukoms VEB C Marhold Halle (Saale) 1959 S 198 201
- Rampoldi A* J of Laryng 1961 Bd 75 S 501 zit Chilaris G & Cojas A
- Schroder K* in Der Augenarzt Bd VI kap 1 Herausgeber K. Velhagen VEB Georg Thieme Leipzig 1964
- Sokolowski St* Otolaryng polska Bd 7 S 301 (1953) Zbl HNO 51 127 (1954/55)
- Ten Doesschate J & M P Lansberg* Ophthalmologica Basel 150 S 66 67 (1955)
- Tille H* Rev otol etc 1931 Bd 15 S 577-583 ref Zbl ges Ophth Bd 40 S 506 (1938)

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THE OCULAR PULSE—TECHNICAL FEATURES

BY

MILTON BEST M D THOMAS A KELLY M S
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Ocular techniques to study carotid occlusive disease include ophthalmodynamometry, carotid compression tonography and ocular pulse measurements. Studies using this latter method have been concerned primarily with the amplitude of the recorded pulse and it has been noted that a reduction in amplitude of the ocular pulse occurs on the side of carotid occlusive disease (Castren *et al* 1964 Bynke 1966 1968a 1968b and 1969 Bynke and Arakawa 1964 Lester 1966 Bron *et al* 1967 Galin *et al* 1967b). Changes in the contour of the ocular pulse recordings have not received much attention although contour analysis has been of great importance in peripheral vascular disease (Winsor 1959).

Ocular pulses recorded from the surface of the eye with a suction cup are similar in all respects to pulses recorded by direct cannulation and reflect the pressure changes occurring in the eye during the cardiac cycle (Lawrence *et al* 1966). This report concerns itself with a consideration of the suction technique used to record ocular pulses and the effects of various physical factors upon the pulse amplitude, peak characteristics and notching.

Methods

The technique utilizes a dome shaped aluminum or plastic suction cup with an outside diameter of 14 mm and an inside diameter of 12 mm presently employed

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in suction ophthalmodynamometry (Galín *et al* 1969a and 1969b) In patients it is placed in contact with the conjunctiva adjacent to the temporal limbus while in rabbits or other experimental animals it is placed directly on the cornea The suction cup is attached to a P23BB Statham transducer by polyethylene tubing (PE 190) with a three way stopcock between the transducer and the suction cup (figure 1) Polyethylene tubing (PE 190) leads from the second arm of the transducer through a three way stopcock to a column of saline that is below the level of the transducer and can provide variable amounts of suction. The entire system is filled with saline All tubes must be free of small air bubbles

The pulses are recorded from both eyes simultaneously on a Beckman type R dynograph with a type 9803 strain gauge coupler and a type 482 dynograph amplifier The transducers are first opened to air and balanced at a sensitivity setting of 0.5 millivolts per centimeter so that a 1 cm deflection equals 2 mm Hg The sensitivity setting on both channels is then increased to 0.05 or 0.1 millivolts per cm and the polarity switched to negative The zero setting is adjusted until a pulse recording appears and is centered on each channel Pulses are recorded at a paper speed of 25 mm per second

In all experiments rabbits weighing between 3 and 4 kg were anesthetized with intravenous pentobarbital 25 to 37.5 mg Proparacaine hydrochloride was used topically Intraocular pressure was controlled with a saline reservoir through a 23 gauge needle inserted into the anterior chamber Either an open or closed manometric system was used and intraocular pressure was continu-

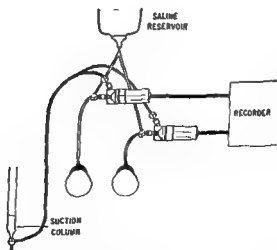


Fig 1

Schematic representation of apparatus to record ocular pulses

ously recorded through a three way stopcock using a P23BB Statham transducer

The suction cup was applied to the cornea while saline was flowing freely through it from a reservoir. When all air bubbles were eliminated from the cup it was firmly applied to the globe and the stopcock was turned to disengage the reservoir and connect the cup to the suction column.

The relationship between intraocular pressure before and after suction equivalent to -40 cm saline was applied is shown in figure 2 where intraocular pressure was varied from 5 to 75 mm Hg using a closed manometric system prior to application of the suction cup

Analysis of Factors

1 The Amount of Suction Figure 3 illustrates the effect of various amounts of suction on the intraocular pressure when a closed manometric system was used to establish an initial intraocular pressure of 21 mm Hg. A linear relationship exists between the level of suction and the subsequent increase of intraocular pressure in the range studied. The highest pressure reached was 46 mm Hg with suction equivalent to -50 cm saline. The amplitude of the ocular pulse bore a similar linear relationship to the level of suction (figure 4). Figures 3 and 4 are plotted from recordings obtained from the same eye and are representative of a series of six eyes.

In order to eliminate the effect of the suction induced increase in intraocular pressure on the amplitude of the recorded pulse, the same experiment was repeated using an open manometric system at intraocular pressures of 21 and 30

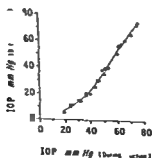


Fig. 2

Relationship between intraocular pressures before and after application of the suction cup at -40 cm saline.

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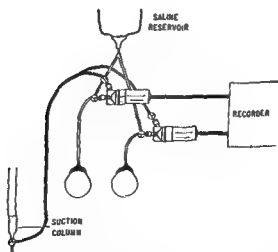


Fig 1

Schematic representation of apparatus to record ocular pulses

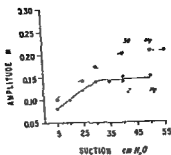


Fig 5
Effect of suction on amplitude of ocular pulse using an open manometric system
at 21 and 30 mm Hg

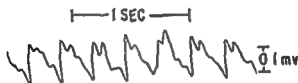


Fig 6
Suction equivalent to ~ 0 cm saline resulted in variable pulses with double peaks
Intraocular pressure was 30 mm Hg (open manometric system)

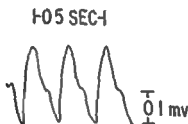


Fig 7
Suction equivalent to -40 cm saline resulted in uniform pulses with single peaks
Intraocular pressure was 30 mm Hg (open manometric system)

varying the height of the saline reservoir. Ocular pulses were recorded in sequences of increasing and decreasing intraocular pressures using either an open or a closed manometric system.

In a second group of rabbits serial records of the ocular pulse were obtained

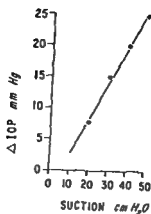


Fig 3

Effect of suction on intraocular pressure Intraocular pressure before suction was 21 mm Hg

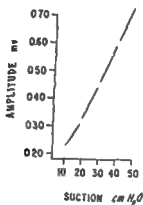


Fig 4

Effect of suction on amplitude of ocular pulse Intraocular pressure before suction was 21 mm Hg

mm Hg The results are shown in figure 5 which indicates that the maximum amplitude of the recorded pulse is obtained at suction levels between -30 and -40 cm saline in an open system

With an open or closed manometric system suction levels below -30 cm saline resulted in double peaking and variability of the ocular pulse (figure 6) At suction levels of -40 cm saline or higher the pulses were uniform and had single peaks (figure 7)

2 The Level of Intraocular Pressure While suction was maintained constant at -40 cm saline intraocular pressure was varied by two techniques In one group of rabbits different levels of intraocular pressure were obtained by

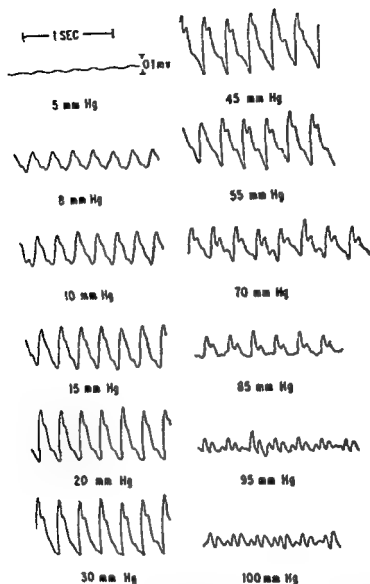


Fig 8

Effect of intraocular pressure on the amplitude and contour of the ocular pulse. Intraocular pressure was established with an open manometric system. Suction was -40 cm saline

Loosening the conjunctiva or removing it under the suction cup when it was placed eccentrically had no significant effect on the contour or the amplitude of the recorded pulse.

during the period of intraocular pressure recovery after prolonged tonometry or massage. Serial measurements of intraocular pressure were made with a Schiøtz tonometer and none of the eyes was cannulated while the pulses were being recorded with the suction cup.

The amplitude and contour of the ocular pulse recorded with the suction cup vary with the level of intraocular pressure whether an open or closed manometric system is used to change intraocular pressure. Figure 8 illustrates the changing form and amplitude of the recorded ocular pulse as intraocular pressure is elevated from 5 to 100 mm Hg in an open manometric system. Notching of the descending limb of the pulse wave was more prominent at high levels of intraocular pressure than at low ones.

The level of intraocular pressure at which the maximum amplitude of ocular pulsation is recorded in a closed manometric system is indicated in figure 9. The two curves represent the minimum (45 mm Hg) and the maximum (55 mm Hg) intraocular pressure at which the ocular pulse of greatest amplitude was recorded in a series of six rabbit eyes. All six curves had the same form and it made no difference whether the measurements were made in an increasing or decreasing sequence of intraocular pressure.

With the open perfusion system the curves relating intraocular pressure and amplitude of the ocular pulse were affected by the sequence in which intraocular pressure was varied. Figure 10 illustrates the results from an eye when the intraocular pressure was first increased and then decreased stepwise between 5 and 105 mm Hg. When intraocular pressure is increased stepwise the curve forms a peak but when measurements are made as intraocular pressure is decreased stepwise there is a distinct flattening of the curve so that the maximum amplitude of the pulse wave is represented by a plateau between 90 and 60 mm Hg.

There is no relationship between the amplitude of the ocular pulse and the level of intraocular pressure when intraocular pressure is lowered by prolonged tonography or massage and the ocular pulse recorded with the suction cup during the recovery period. Figure 11 shows that as the intraocular pressure increases from 3 to 17 mm Hg during the recovery period after prolonged tonometry the amplitude of the ocular pulse remains essentially unchanged. A similar situation exists for intraocular pressures between 6 and 19 mm Hg in the recovery period after massage. This may be due to the relatively small changes in intraocular pressure that occur during the recovery period.

3 Site of Application of the Suction Cup. The amplitude of the ocular pulse was not altered significantly by placing the suction cup on the cornea or sclera alone or straddling both. However the contour of the recorded pulse was affected in about half the rabbits tested. The major effect was an accentuation of the notch on the descending limb of the pulse wave as the suction cup was moved from the central cornea toward the sclera.

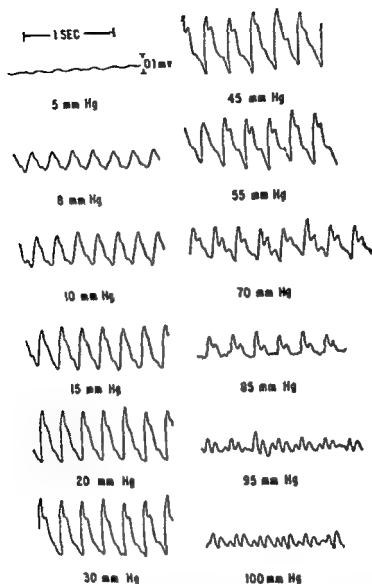


Fig 8

Effect of intraocular pressure on the amplitude and contour of the ocular pulse. Intraocular pressure was established with an open manometric system. Suction was -40 cm saline

Loosening the conjunctiva or removing it under the suction cup when it was placed eccentrically had no significant effect on the contour or the amplitude of the recorded pulse.

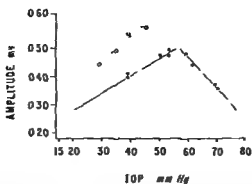


Fig 9

Relationship between amplitude of ocular pulse and intraocular pressure in two eyes. Intraocular pressure was varied with a closed manometric system. Maximum amplitude occurred at an intraocular pressure of 45 mm Hg (interrupted line) in one eye and 55 mm Hg (solid line) in the second eye.

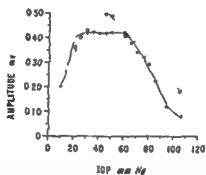


Fig 10

Relationship between amplitude of ocular pulse and intraocular pressure in one representative eye. Intraocular pressure was first increased stepwise (interrupted line) and then decreased stepwise (solid line) between 5 and 105 mm Hg with an open manometric system.

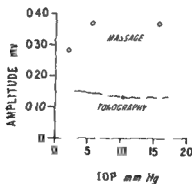


Fig 11

Relationship between amplitude of ocular pulse and intraocular pressure during the recovery period following prolonged tonography (solid line) or massage (interrupted line).

DISCUSSION

Any technique that is used to record ocular pulsation should be easy to perform rapid and of sufficient sensitivity and reliability to give constant and analyzable results. The suction cup technique meets these criteria. The analysis of the results depends upon knowledge of the various factors that can affect the amplitude and contour of the recorded pulse.

The effect of intraocular pressure on the pulse depends upon the methods which are used to vary the level of intraocular pressure and to record the pulse. By recording the pulse through a cannula in the anterior chamber or vitreous Lawrence and Schlegel obtained a variety of curves relating pulse amplitude and intraocular pressure the most common showing a plateau representing the maximum amplitude at intraocular pressures between 40 and 80 mm Hg (Lawrence *et al* 1966). When the procedure was repeated on the same eye the curve no longer had a plateau but formed a peak instead at an intraocular pressure of about 60 mm Hg and they felt this reflected a change in the physical characteristics of the intraocular blood vessels presumably an increase in blood vessel compliance.

If as in this study a suction cup is used to record the ocular pulse and an open perfusion system is used to vary the intraocular pressure the initial curves obtained all peak. A plateau occurs only when amplitude is measured as intraocular pressure is lowered from its elevated starting point. Although an open manometric system damps the amplitude of the recorded ocular pulse it is noteworthy that subjecting the eye to an elevated intraocular pressure with an open system consistently alters the shape of the curve relating intraocular pressure and pulse amplitude recorded with the suction cup in a manner exactly opposite to the curve obtained by direct cannulation experiments. The explanation for this may be that there is a marked increase in ocular rigidity at all levels of intraocular pressure after the eye has been stretched by a high intraocular pressure (Ridley 1930). This would result in a greater amplitude of the ocular pulse as measured by direct cannulation since this technique measures the true pressure pulse. The amplitude of the ocular pulse as measured with a suction cup however would be decreased since this technique measures movements of the cornea into and out of the suction cup (Suzuki 1962).

In the non cannulated eye the amplitude as well as the contour of the suction recorded ocular pulse is not affected by lowering the intraocular pressure by tonography or massage until the intraocular pressure reaches levels of 4 to 6 mm Hg or less. This means that during the procedure for recording ocular pulses the massage effect of the suction cup will have no effect on the amplitude or contour of the recorded pulse unless the procedure is unduly prolonged. On the other hand elevating the intraocular pressure above normal levels has

a similar effect on the suction recorded ocular pulse in a cannulated or non cannulated eye

The effect of variations of the amount of suction on the contour of the recorded pulse is very important. Below suction levels of -30 cm saline the recorded pulse wave contains numerous notches on both the ascending and descending limbs with many double peaks. In addition there is extreme variability in both the amplitude and contour of the ocular pulse as recorded from a single eye. These findings occur in both open and closed manometric systems indicating that the variability is not associated with changes in intraocular pressure. At levels of suction greater than -30 cm saline the recorded pulses are simpler in form with a definable peak and one or two notches usually limited to the descending limb. Also the amplitude and contour of the recorded pulses are consistent. A level of -40 or -50 cm saline is sufficient to produce a consistent recording of the ocular pulse which can be studied with relative ease.

One of the most common causes of variation in the contour of the ocular pulse is a change in the position of the suction cup. The simplest technique in rabbits is to place the cup centrally on the cornea. If the cup is moved toward the limbus no alteration in the recorded pulse occurs until the edge of the cup straddles the limbus. At this point there will often be an accentuation of the notch that appears on the descending limb of the pulse wave. This effect usually disappears when the suction cup is placed entirely on the sclera. Looseness of the conjunctiva appears to have no effect on the amplitude or contour of the recorded pulse.

In the non cannulated eye of the rabbit the ascending limb of the suction recorded pulse wave is usually free of notches or deflections whereas the descending limb usually has a well defined notch or deflection. Using an open manometric system this study shows that at intraocular pressures below 30 mm Hg and at intraocular pressures 50 mm Hg or higher the notch on the descending limb is absent or not prominent. Changes in notching or deflection may be of importance in occlusive vascular disease. Therefore -40 cm saline was chosen as the appropriate suction level for studying induced carotid lesions in rabbits since it resulted in intraocular pressures between 35 and 40 mm Hg in most animals. At this level of suction slippage of the suction cup from the center of the cornea was minimal.

The apparatus and technique described in this study have been used on many human subjects (Galín *et al* 1967a). Consistent ocular pulses can be recorded rapidly with a minimum of discomfort to the patient. In addition this technique does not have the disadvantage of displacing the globe posteriorly into the orbit that has been described with other instruments (Bynke 1968c).

Summary

A technique is described for recording ocular pulses using a suction cup. The contour and amplitude of the recorded pulse are affected by the amount of suction, the level of intraocular pressure and the site of application of the suction cup. The most easily analyzed and consistent pulses are obtained with suction equivalent to -40 cm saline which induces an intraocular pressure between 35 and 40 mm Hg. Criteria of importance in analysis of ocular pulse waves include amplitude, notching on the ascending and descending limbs and peak characteristics. The apparatus and technique described result in consistent ocular pulse recordings that can easily be analyzed for the above characteristics.

Acknowledgment

Photographs were supplied by Mr Morris Moritz, Bird S Coler Hospital.

References

- Bennett J, Knox D L & Gaasterland D. Tonographic studies in carotid occlusive disease. *Brit J Ophthalmol* 1966; 51: 577.
- Bynke H G. Screening diagnosis of carotid occlusion by means of oculosphygmography. *Neurology* 1966; 16: 383.
- Bynke H G. Further estimation of the oculosphygmography as a diagnostic method in carotid occlusive disease. *Acta Ophthalmol* 1968a; 46: 92.
- Bynke H G. A study of the amplitude of the corneal pulse at experimental carotid occlusion in rabbits. *Acta Ophthalmol* 1968b; 46: 306.
- Bynke H G. Influence of intraocular pressure on the amplitude of the corneal pulse. *Acta Ophthalmol* 1968c; 46: 1135.
- Bynke H G. Further studies on the ocular pulse in rabbits at experimental carotid occlusion and at loading of the bulb. *Acta Ophthalmol* 1969; 47: 314.
- Bynke H G & Krakau C E T. A handy instrument for oculosphygmography with clinical results. *Ophthalmologica* 1964; 148: 36.
- Carlsson J I & Lankinen P. A new method of diagnosing carotid disease. *Acta Ophthalmol* 1964; 42: 19.
- Carlsson M A, Dodick J M & Best M. Ocular manifestations of cranial insufficiency. In: Proc 2nd International Congress of Neuro Genetics and Neuro Ophthalmology (the World Federation of Neurology, Montreal, Canada, September 17-22, 1967a).
- Carlsson M A, Podrigue Barros R, Pola R & McLaren J M. Cerebrovascular insufficiency. *Trans Amer Acad Ophthalmol Otolaryng* 1967b; 41: 119.
- Carlsson M A, Barros R & Cavero R. Ophthalmodynamometry using suction. *Arch Ophthalmol* 1968a; 41: 491.
- Carlsson M A, Barros R, Cavero R & Best M. Compression and suction ophthalmodynamometry. *Amer J Ophthalmol* 1968b; 66: 359.

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References

- Brown I. J., Knox D. L. & Gaasterland D. Tonographic studies in carotid occlusive disease. *Brit J Ophthalmol* 1966 51 517.
- Bynke H. G. Screening diagnosis of carotid occlusion by means of oculosphygmography. *Neurology* 1966 16 353.
- Bynke H. G. Further estimation of the oculosphygmography as a diagnostic method in carotid occlusive disease. *Acta Ophthalmol* 1965a 6 92.
- Bynke H. G. A study of the amplitude of the corneal pulse at experimental carotid occlusion in rabbits. *Acta Ophthalmol* 1965b 46 806.
- Bynke H. G. Influence of intraocular pressure on the amplitude of the corneal pulse. *Acta Ophthalmol* 1965c 46 1132.
- Bynke H. G. Further studies on the ocular pulse in rabbits at experimental carotid occlusion and at ligation of the bulb. *Acta Ophthalmol* 1969 4 514.
- Bynke H. G. & Arakawa C. E. T. A handy instrument for oculosphygmography with some clinical results. *Ophthalmologica* 1964 149 367.
- Ellerstein J. A. & Lavinainen P. A new method of diagnosing carotid disease. *Acta Ophthalmol* 1964 4 239.
- Calvin M. A., Dulick J. M. & Best H. Ocular manifestations of cranial insufficiency. In: Second International Congress of Neuro Genetics and Neuro Ophthalmology. The World Federation of Neurology, Montreal, Canada, September 17-22, 1967a.
- Calvin M. A., Rodriguez Barrios R., Fels R. & McLean J. M. Cerebrovascular insufficiency. *Trans Amer Acad Ophthalmol Otolaryng* 1967b 1 119.
- Ellerstein J. A., Baras I. & Cavero R. Ophthalmodynamometry using suction. *Arch Ophthalmol* 1969a 51 494.
- Ellerstein J. A., Baras I., Carter R. & Best H. Compression and suction ophthalmodynamometry. *Amer J Ophthalmol* 1969b 6 353.

- Lawrence C & Schlegel W* 4 Ophthalmic pulse studies I Influence of intraocular pressure *Invest Ophthal* 1966 5 515
- Lester H A* Ocular oscillometry in cerebrovascular disease *Arch Ophthal* 1966 16 391
- Ridley F* The curve of distensibility of the sclera *Brit J Exp Path* 1930 11 230
- Suuki I* Corneal pulsation and corneal pulse waves *Jap J Ophthal* 1963 6 190
- Winsor T* Peripheral vascular disease an objective approach Springfield Illinois, 1959 Charles C Thomas

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PIGMENTGESCHWULSTE DER BINDEHAUT Nebst kritischer Bemerkungen zur Röntgenbestrahlung

VON

A HEYDENREICH

Pigmentgeschwulste gehören zu den besonders malignen Tumoren und verdienen deshalb gesteigerte Aufmerksamkeit. Im Bereich des Auges begegnen wir ihnen besonders in der Uvea, aber auch im äusseren Teil des Auges, vor allem in der Conjunktiva. Die Prognose der Uveamelanome wird dabei im allgemeinen wesentlich günstiger eingeschätzt als die der Haut- und Schleimhautmelanome (Wright 1949).

Während jedoch die Uveamelanome meist erst in fortgeschrittenem Stadium diagnostiziert werden, wenn Sehstörungen auftreten oder sie rein zufällig bei einer routinemässigen Ophthalmoskopie erkannt werden, sind die Bindehautpigmenttumoren dem Blick sofort zugänglich und führen den Patienten schon aus kosmetischen Gründen frühzeitig zum Arzt. Sie erfordern in jedem einzelnen Fall gründliche Überlegung des notwendigen therapeutischen Vorgehens und Handelns, besonders da sie in vielen Fällen zunächst jahrelang als sehr gutartig erscheinen und nur gelegentlich zum Teil aus unbekannten Gründen maligne entarten.

Nach Thiel (1965) können wir drei Arten von Pigmenttumoren bzw. -anomalien im Bereich der Konjunktiva unterscheiden:

1. Die *Melanosis*. Sie beginnt klinisch als kleiner flacher Pigmentfleck mit feiner granularer Pigmentation, die sich allmählich über die ganze bulbare und palpebrale Konjunktiva, die Karunkel, die Hornhaut und Lider ausbreiten kann. Gegebenenfalls findet man auch eine Melanosis im Inneren des Auges (Iris).

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- Lawrence C & Schlegel W A* Ophthalmic pulse studies I Influence of intraocular pressure Invest Ophthal 1966 5 515
- Lester H A* Ocular oscillometry in cerebrovascular disease Arch Ophthal 1966 16 391
- Ridley F* The curve of distensibility of the sclera Brit J Exp Path 1930 11 230
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Aderhaut) Histologisch gleich das Bild zunächst der einfachen Pigmenthypertrophie (s u) später findet man proliferierende pigmentierte Zellen sub und intraepithelial mit entzündlichen Reaktionen an den Wucherungsgrenzen

2 *Naevus pigmentosus* Er tritt klinisch als leicht erhabenes Gebilde in der Konjunktiva auf und enthält meistens reichlich Pigment Histologisch findet man die typischen Naevuszellnester mit epithelähnlichen Zellen und blaschenförmigen Kernen Die Naevuszellen sind meist pigmentarm die darüberliegende Epidermis und das umgebende Bindegewebe stark pigmentiert Nach Albertus handelt es sich um eine "dysontogenetische Geschwulst" im Sinne eines Hamartoms Sie können angeboren oder erworben sein und entstehen meist im ersten Dezenium

3 *Melanom* die eindeutig bösartige Geschwulst Sie ist klinisch durch rasches Wachstum Prominenz und Gefassreichtum und histologisch durch karzinomatösen oder sarkomatösen Zellaufbau gekennzeichnet Im allgemeinen entwickelt sie sich erst im 4 und 5 Lebensjahrzehnt

Als 4 Gruppe wird vielfach das juvenile Melanom (Spitz 1948) abgegrenzt das sich klinisch durch einen gutartigen Verlauf auszeichnet histologisch jedoch als auffallend maligne erscheint Eine Differenzierung vom malignen Melanom ist auf Grund mehrkerniger Riesenzellen die dem Toutontyp ahnelt, gewisser Einformigkeit und mangelndem Pleomorphismus der Zellen fast völligem Fehlen von Pigment und naevuszellartigen Strukturen möglich Es wird nicht nur im Kindesalter sondern in etwa 15 % der Fälle auch bei Erwachsenen beobachtet (Allen 1960) Thiel hält eine strenge Abgrenzung des juvenilen Melanoms von den Pigmentzellnaevi für nicht berechtigt Infolge des geringen Pigmentgehaltes ist klinisch eine Verwechslung mit Angiomen teleangiektatischen Granulomen möglich

Schliesslich muss man von diesen 4 Gruppen noch die einfache Pigmenthypertrophie abtrennen die gelegentlich auch an eine maligne Pigmententartung denken lassen kann besonders wenn es zu einer – auch für den Patienten auffallenden und zunehmenden Pigmentierung im Bindehautbereich kommt wie z B bei Pat Erika St 14 J 1963

Anamnese Seit 12 Jahren von den Eltern im rechten Auge ein Muttermal beobachtet, das grosser geworden sei Seit 2 Jahren auch am linken Auge ein Muttermal beobachtet

Befund Beiderseits befindet sich nasal in Nahe des Limbus in der Conjunctiva bulbi eine Pigmentansammlung (Abb 1) An der Spaltlampe erkennt man zusätzlich zahlreiche Pigmentzellen fast zirkular am Limbus Exzision des Pigmentfleckes rechts

Histologisch Bindehautstück mit stark pigmentierten Zellen im basalen Anteil der Epithelschicht Einzelne Chromatophoren im subepithelialen Gewebe keine Naevuszellen (Abb 2) Befund 23.6.1966 Rechts zarte Bindehautnarbe mit einzelnen Pigmentkörnchen Links unveränderter Pigmentfleck

Die einfache Pigmenthypertrophie stellt eine vermehrte Ansammlung von Pigmentzellen dar die normalerweise am Limbus corneae und gelegentlich



Abb 1

Pigmenthypertrophie am rechten Auge (Pat Erika St.)



Abb 2

Histologischer Befund von Abb 1 H E Färbung

auch in der angrenzenden *Conjunctiva bulbi* bei allen pigmentierten Tier- und Menschenrassen und in etwa 2/3 der Fälle auch in geringem Umfange bei der mitteleuropäischen Bevölkerung vorkommen und in bestimmten Lebensphasen (Pubertät Gravidität) eine Vermehrung bzw. Hyperpigmentation zeigen können. Histologisch handelt es sich vor allem um Pigmentzellen epithelialen Typs in der Basalschicht des Epithels und um einzelne Chromatophoren im mesenchymalen subepithelialen Gewebe. Sie werden auch in ihren Vorstufen (Propigment) besonders gut mit der Methode nach Masson Hamperl dargestellt (s. auch Heydenreich 1968).

Pigmentnaevi und Melanosis können sich vergrößern und den Eindruck des bösartigen Wachstums hervorrufen, ohne dass histologisch schon eine Maligni-

tät nachzuweisen ist. Es handelt sich dabei um Einlagerung von Pigment in die Umgebung und nicht um Destruktion des benachbarten Gewebes. Eine maligne Entartung ist aber durchaus möglich, wobei klinisch eine Zunahme der Pigmentierung, höckerige Gewebswucherung, Gefässreichtum und Hyperämie (Abb. 3) und nach Thiel eine Trübungszone in der angrenzenden Hornhaut ähnlich dem Arcus lipoides hinweisend sind. Histologisch fällt eine erhebliche Wucherung, Entdifferenzierung der Crundelemente mit abnormer Zellgrösse, Vakuolenbildung, Kernvermehrung und -atypien und destruktive invasive Proliferation auf. So gibt es für das Zustandekommen eines Melanoms drei Möglichkeiten: Entartung einer Melanosis, Entartung eines Pigment Naevus und Entstehung einer primären malignen Pigmentgeschwulst auf vorher unveränderter Haut bzw. Bindehaut. Als Urche der Entartung werden vielfach geringfügige Traumatisierungen (auch Probeexzisionen!) oder entzündliche Veränderungen (akuter heftiger Bindehautl. atarrh) angenommen. Endokrine Faktoren (Pubertät, Schwangerschaft, ACTH Behandlung) können als Wachstumsreiz wirken (Cook 1952, Thiel 1965). Häufig fehlen jedoch aussere Anhaltspunkte, so dass Thiel u. a. die Entstehung aus primär vorhandenen atypischen Melanozyten annehmen.

Die längere Beobachtung mehrerer pigmentierter Bindehauttumoren mag auf die Problematik der klinischen und histologischen Diagnostik und der daraus abgeleiteten Therapie hinweisen (s. auch Lapp 1969).

Bei einem stationären augenärztlichen Krankengut von 12 526 Patienten



Abb. 3

Pigmentzellnaevus am linken Auge (Fall 2, Tab. 1)

(1955 1965) fanden sich 440 Tumorträger davon hatten 24 Patienten Tumoren der Bindehaut und Karunkel bei 12 dieser Patienten handelte es sich um Pigmenttumoren 8 Naevi pigmentosi und 4 Melanome (s. Tab. 1 und 2)

Die 8 *Pigment ellnacci* bestanden aus 2-5 mm grossen meist stark pigmentierten leicht erhabenen Knoten die in Nähe des Limbus bzw. der Karunkel sasssen Häufig waren die umgebenden Gefässe erweitert Bei 3 Fällen tauchte klinisch der Verdacht eines malignen Melanoms auf besonders da bei Fall Nr. 1 ein stärkeres Umgebungsoedem bestand bei Fall Nr. 4 während einer Gravität die Pigmentierung stark zunahm und bei Fall Nr. 5 die Geschwulst relativ gross (3 mm) und stark durchblutet war Auch histologisch bestand Melanomverdacht Das Alter der Patienten lag zwischen 5 und 32 Jahren die Tumoren wurden von den Patienten meistens erst seit $\frac{1}{2}$ 1 Jahr gelegentlich schon seit 3-4 Jahren bemerkt Die Therapie bestand in allen Fällen in einer chirurgischen Exstirpation bei Fall 5 und 6 in einer zusätzlichen Röntgenvorbestrahlung (3400-8000 R) Ein Rezidiv bzw. maligne Entartung wurden in der Nachbeobachtungszeit von 3-10 Jahren nicht festgestellt

Die 4 malignen Melanome zeigten demgegenüber ein ganz anderes Verhalten So konnte die Diagnose einer Malignität anhand des progressiven Wachstums der Grösse des tumorösen Prozesses und des Gefässreichtums schon klinisch eindeutig gestellt werden In 2 Fällen (Nr. 3 und 4) war auch die von Thiel beschriebene randnahe Hornhauttrübung vorhanden Das Alter der Patienten betrug bei der Aufnahme in der Klinik 34 bis 42 Jahre 3 Patienten wussten dass sie schon seit 10-40 Jahren einen kleinen Pigmentfleck am Auge besaßen nur bei 1 Patienten (Nr. 4) wurde der Tumor 3 Wochen vor der Aufnahme zufällig bemerkt Bei 2 Fällen erfolgte Exstirpation des Tumors mittels Diathermie und Röntgennachbestrahlung (8000-8500 R) in 1 Fall alleinige Röntgenbestrahlung (6150 R) und in 1 Fall (Nr. 2) primäre Enukleation mit anschliessender Röntgentiefenbestrahlung (4500 R) In 3 Fällen (Nr. 1 u. 2) trat trotzdem innerhalb von 2 Jahren Exitus letalis ein bei Fall Nr. 2 ging vorher noch eine intensive Röntgenbestrahlung und Exenteratio orbitae vor aus $\frac{1}{4}$ Jahr vor dem Exitus letalis kam es zu einer Melanomaussaat auf der gleichen Gesichtseite (Abb. 1) In den beiden übrigen Fällen trat innerhalb der nächsten 6 bzw. 8 Jahre kein Rezidiv auf allerdings erblindeten die Augen offenbar als Folge der Röntgenbestrahlung Bei Fall Nr. 4 entwickelte sich eine Röntgenkatarakt und Sekundär Glaukom Das Auge wurde 4 Jahre später wegen Beschwerden enukleiert der histologische Befund ergab kein Tumor rezidiv nur fibroses Narbengewebe im Bereich des ursprünglichen Tumorsitzes

Die hier erhobenen Befunde bestätigen erneut dass die Diagnose der Benignität eines Pigmenttumors so lange keine Schwierigkeiten bereitet wie der Tumor nur 3-4 mm gross ist kein Wachstum zeigt und im jugendlichen Alter beobachtet wird Wesentlich schwieriger wird es bei Zunahme der Pigmentie

Tabelle 1

Krbl Nr	Geschl	Alter	Zeitdauer	histol Besonderh	Behandlung	Besonderheiten	Nachbeobachtung
253/1956 klinisch Melanomverdacht	♂	5 J	4 J	Pigmentzellnaevus Melanomverdachtig	Exstirpation	3 mm grosser Irgmentknoten mit starkem Umgebungsodem und Gefasszeichnung	10 Jahre
708/1960	♂	20 J	1 J	Pigmentzellnaevus	Exstirpation	4 mm grosser Knoten am Kor per mehrere Pigmentnaevi	ungekannt
605/1961	♀	7 J	3 J	Pigmentzellnaevus	Exstirpation	3 mm grosser Knoten mit vermehrter Gefasszeichnung	5 Jahre
220/1962 klinisch Melanomverdacht	♀	21 J	2 3 J	Pigmentzellnaevus Melanomverdachtig	Exstirpation mittels Diathermie	Graviditas Mens VI In letzten Wochen Zunahme der Pigmentierung 4 5 mm Grosse	7 Jahre
1306/1963 klinisch Melanomverdacht	♂	32 J	3 J	Pigmentzellnaevus mit chronischer Entzündung	8000 R OD Ro Bestrahlung Exstirpation	5 mm grosser Tumor stark durchblutet Verdacht auf Melanomat Nach 3 J beginnen die Ro Cat Nach 4 J Chorio retinitis mit grossem zentralem atrophischen Aderhaut Netzhaut Herd kleine Netzhautblutungen und circumferenzielle Herde und Gefassneubildungen in der Umgebung SFT 1 168 AST 400	4 Jahre

1314/1963	♀	14 J	1 J	Igmenzellnaevus mit cl. ron. Entzündung am Kande	Ro Bestrahlung . 4 mm grosser Knoten auf der 5400 R OD Karunkel Exstirpation	4 Jahre
1317/1963	♂	6 J	1/2 J	Igmenzellnaevus mit chronischer Entzündung	Exstirpation 9,5 mm grosser Knoten mit vermehrter Gefässzeichnung am Kande	3 Jahre
1104/1965	♂	01 J	1/2 J	Igmenzellnaevus	Exstirpation 3 mm grosser Knoten	3 Jahre

Tabelle 2

Krbl Nr	Geschl	Alter	Zeitdauer	histol Besonderh
644/1958	♀	54 J	Seit 10 J kleiner roter Fleck im letzten 1/2 J vergrossert	Malignes Melanom
75/1959	♂	72 J	Seit 40 J nach kriegsver- letzung kleinen pigmen- tierten Fleck bemerkt Seit 1/2 J Vergrosserung	Naevuszellnester und typisches malignes Mela- nom
69/1960	♀	67 J	Seit 20 J stechnadelkopf- grosser Tumor seit 6 J Vergrosserung und Pig- mentierung	Malignes Melanom
301/1963	♀	68 J	Seit 3 Wochen zufällig bemerkt	kein Befund

rung z H während einer Gravidität (Fall Nr 4 Tab 1) und bei auffallender
 Gefasszeichnung und Grossenzunahme in derartigen Fällen kann unter Um-
 standen auch histologisch keine klare Abgrenzung gegenüber einer Malignität
 erfolgen (Fall Nr 1 4 und 5 Tab 1) Andererseits ist bei Pigmenttumoren der
 Bindehaut im höheren Lebensalter immer mit einer Malignität zu rechnen wie
 die wenigen von uns beobachteten Fälle sehr eindrucksvoll zeigen Trotz thera-
 peutischer Massnahmen kamen 2 der 4 Patienten innerhalb von 2 Jahren ad
 exitum Fall Nr 2 mit einer sichtbaren metastatischen Aussaat auf der gleichen

Behandlung	Besonderheiten	Nachbeobachtung
Ro Bestrahlung 8000 R OD Exstirpation	kirschgrosser Tumor im nasalen Lidwinkel	Nach 2 Jahren †
Enukleation Ro Bestrahlung 4500 R OD	Bohnergrosse rote Ge- schwulst, die den halben Limbus umgreift, kein Übergreifen auf die Con- junktiva tarsi	Nach 1 Jahr Rezidiv in der Augenhöhle Ro Vorbe- strahlung 500 R, Exentera- tio orbitae Nachbestrah- lung der Höhle (Tiefen- therapie 3000 R) und der Lymphdrüsen 3500 R OD Nach 2 1/2 J Aussaat von Melanomknoten linke Ge- sichtsseite. Ro Bestrahlung 3500 R OD †
Exstirpation Ro Bestrahlung 8500 R OD	Erbsengrosse braunlicher Tumor mit vielen Gefässen u. randnaher Hornhaut- trübung Beginnende Cat- aractus In den Armen viele Warzen	8 Jahre Auge ist erblindet
Ro Bestrahlung 6150 R. OD	5 mm grosser hellbrauner an 1 Stelle dunkelbraun pigmentierter Tumor am Limbus mit vielen Gefässen und randnaher Hornhauttrübung	Nach 2 Jahren fortge- schrittene Cataract und Sekundär Glaukom Amaurose 6 Jahre Beob- achtung Nach 4 Jahren Enuklea- tion. Histol. kein Anteil mehr von Tumorzellen

Gesichtsseite – Bemerkenswert ist dass bei 3 der beschriebenen malignen Me-
lanome schon seit 10–40 Jahren ein Pigmentfleck in der Konjunktiva beob-
achtet wurde und in Fall 2 auch histologisch der Charakter eines Pigmentzell-
naevus nachzuweisen war. Diese Beobachtungen weisen erneut daraufhin wie
entscheidend wichtig es ist dass auch kleine Pigmenttumoren zu einem Zeit-
punkt entfernt werden wo sie noch als benigne an zu sehen sind also möglichst
im jugendlichen Alter. Dabei kann die einfache Exstirpation – eventuell er-
gänzt durch Diathermie oder gleichzeitige Kryobehandlung – genügen wie sich

Tabelle 2

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Ro Bestrahlung 7150 R OD	5 mm grosser hellbrauner an 1 Stelle dunkelbraun pigmentierter Tumor am Limbus mit vielen Gefässen und randnaher Hornhauttrübung	Nach 2 Jahren fortge- schrittene Cataract und Sekundär Glaukom Amaurose 6 Jahre Beob- achtung Nach 4 Jahren Enuklea- tion. Histol kein Anteil mehr von Tumorzellen

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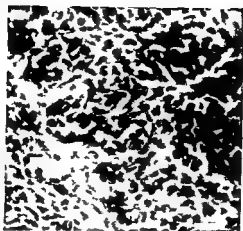


Abb 4

Histologischer Befund vom Pigmentzellnaevus mit typischen Naevuszellnestern
(Fall 7 Tab 1)



Abb 5

Melanom im äusseren Lidwinkel und am Limbus Durch Röntgenbestrahlung geheilt
(Fall 4 Tab 2)

aus der längeren Überwachung unserer Patienten mit Pigmentzellnaevi (Tab 1) ergibt. Besteht die Möglichkeit der β Bestrahlung so ist sie auf Grund ihrer guten Ergebnisse vorzuziehen.

Noch einige Bemerkungen zur Röntgentherapie maligner Tumoren im äusseren Augenbereich. Um mit der konventionellen Röntgenbestrahlung



Abb 6

Rezidivtumor nach Enukleation und Röntgennachbestrahlung (Fall 2 Tab II)



Abb 7

Metastasenausssaat linke Gesichtseite $\frac{3}{4}$ Jahr nach Exenteratio orbitae (Fall 2 Tab 9)

(Chaoul'sche Nabbestrahlung) bei epibulbaren Melanomen einen überzeugenden Erfolg zu erzielen sind sehr hohe Dosen von möglichst 6 8000 R Oberflächen dosis (OD) notwendig. Da uns keine andere Strahlenbehandlung zur Verfügung stand wurde sie bei den 4 malignen und 2 fraglich benignen Fällen eingesetzt. In 2 Fällen konnte der Exitus letalis nicht verhindert werden da wahrscheinlich schon Metastasen bestanden die allerdings zur Zeit der Behandlung klinisch nicht ermittelt wurden. In den übrigen Fällen konnte ein ausreichender therapeutischer Erfolg quoad vitam bei 6 – bis 8 jähriger Nachbeobachtung festgestellt werden – allerdings nicht quoad visum.

Bei 5 der 6 bestrahlten Fälle kam es in den folgenden 2 4 Jahren zur prak

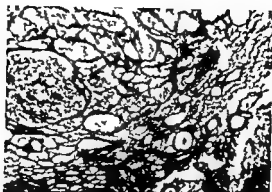


Abb 8

Histologischer Befund des Primartumors Gomori Färbung (Fall 2 Tab 2)

tischen Erblindung der Augen in 1 Fall musste wegen Schmerzen und Sekundarglaukoms das bestrahlte Auge enukleiert werden – Tumorzellen waren histologisch nicht mehr nachzuweisen

Bei einem Fall (Nr 5 der Tab 1) entwickelten sich Veränderungen wie sie heute nur noch sehr selten gesehen werden und bei Unkenntnis der Vorgeschichte zu differentialdiagnostischen Schwierigkeiten führen können. So wurde 3 Jahre nach der Röntgenbestrahlung (8000 R OD in 36 Sitzungen) eine beginnende Röntgenkatarakt mit hinterer Schalentrubung und oberflächlicher Hornhauttrübung mit Gefasseinsprossung sowie Irisatrophie temporal in Nähe des bestrahlten Bezirkes d. h. des früheren Sitzes des Tumors beobachtet. Am Fundus bestand das Bild einer Periphlebitis retinae mit Einscheidung einiger kleiner Venenäste und winzigen Blutungen in der Umgebung im temporalen und oberen Bereich. 1 Jahr später hatte sich am Fundus im Bereich des hinteren Pols ein mehrere papillendurchmessergrößer atrophischer Aderhaut-Netzhautherd entwickelt, der von breiten circinataartigen Degenerationen umgeben war. In der gesamten Fundusperipherie befanden sich einzelne kleine retinale Blutungen mit mehreren feinen Gefäßneubildungen und groberen weissen Einscheidungen der Vena temporalis inferior und einzelner kleiner Venenäste (Abb 9). Die Hornhaut, Iris und Linsenveränderungen hatten kaum zugenommen. Der Visus betrug noch 1/20.

Ähnliche Strahlenschaden am Fundus wurden von *Burch-Hirschfeld* 1904, *Hoffmann* 1930, *Schmidt* 1937, *Fry* 1952, *Schreck* 1953, *Winter u. Mitarb.* 1958, *Fleming* 1962, *Chee* 1968 u. a. mitgeteilt. Sie traten nach Röntgenbestrahlungen bulbärer, orbitaler und palpebraler Tumoren, aber auch nach Hypophysenbestrahlungen auf. Meistens werden die Schäden am Fundus allerdings nicht diagnostiziert, da durch eine Strahlenkatarakt der Einblick in den hinteren Augengrundschnitt gestört ist und das Auge an einem Sekundarglaukom zugrunde geht.



Abb 9

Röntgenspatschaden am Augenhintergrund mit atrophischem Aderhauterd am hinteren Pol und circinataartigen Degenerationen in der Umgebung Gewebeeinscheidung der Vena temp inferior (Fall 5 Tab 1)

Es ist deshalb sehr zu erwägen ob man heute noch eine Röntgenbestrahlung mit Oberflächendosen von 8000 R und mehr am Auge selbst anwenden soll. Eine sofortige Enukleation bzw Exenteratio orbitae kann dem Patienten viele Beschwerden ersparen und die Möglichkeiten eines günstigen Ausganges quoad vitam steigern. Die weitere Entwicklung der Strahlentherapie lässt erwarten dass derartige Schaden am Auge auch bei der Hypophysenbestrahlung immer seltener werden. Für epibulbare Tumoren hat die β Bestrahlung einen wesentlichen Fortschritt gebracht da sie eine starke Oberflächenwirkung mit schnellem Dosisabfall zur Tiefe besitzt und die hinteren Augenabschnitte kaum gefährdet. Mallet (1965) empfiehlt die Behandlung mit Radiumkörnern in Form von seeds (4000 R innerhalb von 48 / 2 Stunden) wobei allerdings eine Strahlenkatarakt in Kauf genommen wird die 3 bis 5 Jahre später zu operieren ist.

Zusammenfassung

Der Naevus pigmentosus ist die häufigste Pigmentgeschwulst im Bereich der Bindehaut und wird vor allem im jugendlichen Alter beobachtet. Da er des öfteren maligne entartet ist seine frühzeitige Entfernung dringend erforderlich. Das maligne Melanom tritt meistens im Alter auf. Trotz Totalexstirpation bzw Enukleation und Exenteratio orbitae und Röntgenbestrahlung ist der letale Ausgang nicht immer zu verhindern. Die Röntgenbestrahlung epibulbarer Tumoren ist wegen ihrer Gefahren für den Bulbus kein adäquates Verfahren.

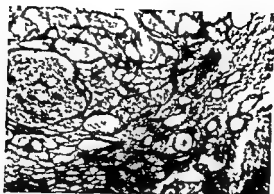


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DENDRITIC (HERPETIC) KERATITIS

IV Follow Up Examination of Corneal Sensitivity

BY

M S NORN

The corneal sensitivity may be impaired in various diseases of the cornea e.g. corneal dystrophy (Fuchs' endothelial dystrophy, Groenow's macular dystrophy, rarely the granular) following zoster ophthalmicus, in trachoma at the site of blood vessel invasion, after cataract extraction at the site of the transected nerves etc.

Corneal ulcer is associated with hyperaesthesia, whereas in the presence of attending corneal oedema hypaesthesia is found.

When contact lenses are fitted a considerable reduction of the corneal sensitivity indicates that the lens ought to be modified.

As is well known the cornea is often hypaesthetic after herpetic keratitis. According to *Thygeson et al.* the impaired sensitivity is an important diagnostic sign, the sensitivity being always reduced in these cases, often even greatly so.

Sclerim on the other hand has shown the sensitivity to be normal in cases of purely epithelial stellate keratitis. Purely epithelial dendritic keratitis is certainly associated with impaired sensitivity during an eruption, but the sensitivity returns to normal in the course of about 8 months. The sensitivity becomes more

Aided by a grant from *Cykelhandler P. Th. Rasmussen og hustru Alma Rasmussen's* *idelegat*.

Read before the Danish Ophthalmologic Society 27.9.1969.

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mehr Es wird in diesem Zusammenhang über schwere Schäden am Augen hintergrund berichtet

Literatur

- Albertini v A* Histologische Geschulst Diagnostik Thieme Verl Stuttgart 1955
- Allen A C* Juvenile Melanomas of children and adults and Melanocarcinomas of children Arch Derm Syph 82 325 (1960)
- Birch Hirschfeld* Die Wirkung der Rontgen und Radiumstrahlen auf das Auge Graefes Arch 59 229 (1904) u 66 104 (1907)
- Chce P H Y* Radiation retinopathy Amer J Ophthalm 66 860 (1968)
- Cook C A* The life history of pigmented naevi Trans Ophthalm Soc U Kingd 11, 257 (1952) ref Zbl Ophth 60 97 (1953)
- Fleming A O* Some observations of the effect of massive radiation on the normal human eye Trans canad ophthal Soc 25 251 (1962) ref Zbl Ophthalm 91 183 (1964)
- Fry W L* Secondary glaucoma cataract and retinal degeneration following radiation Trans amer acad ophth a Otolaryng 56 988 (1952) ref Zbl Ophthalm 60 307 (1964)
- Heydenreich A* , Mikroskopisch histologische Untersuchungsmethoden VEB Thieme Leipzig 1968
- Hoffmann W* Netzhautveränderungen nach Rontgenbestrahlung 48 Vers O G Heidelberg 1930 296 u 58 Vers O G Heidelberg 1953
- Knupfer N* Seltene Rontgenshaden am Auge und in seiner Umgebung Klin Mbl Augenhk 116 66 (1950)
- Lapp A* Über Pigmentumoren der Bindehaut Dissertation Jena 1969
- Mallet* Die Behandlung des bösartigen Melanoms der Bindehaut und des Limbus Klin Mbl Augenhk 146 114 (1965)
- Schmidt J* Röntgenshädigung des Auges Klin Mbl Augenhk 98 686 (1937)
- Schreck* Disk Bem zu Hoffmann 58 Vers O G Heidelberg 1953
- Thiel R* Krebsprobleme in der Augenheilkunde Buch d Augenarztes Beih der Klin Mbl Augenhk Heft 44 (1965)
- Winter F C Reinhardt P R & Maden J* Ocular effects of high intensity gamma radiation on the cat Amer J Ophthalm 46 114 (1958) ref Zbl Ophthalm 46 989 (1959)
- Wright C J E* Prognosis in cutaneous and ocular malignant melanoma J of Path 61 507 (1949) ref Zbl Ophth 55 45 (1951)

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impaired in relation to deeper herpetic keratitis and remains at this low level (27 eyes observed for up to 12 months)

According to *Gundersen* the sensitivity is not impaired at the start of the first attack but the impairment develops in the course of this

The cause of the impaired sensitivity has been discussed

Reiser on histological examination of rabbit corneae found no primary damage of the corneal nerves at the acute stage. Here and there he noticed it is true a coat of leucocytes round the nerves but similarly may be seen in other forms of keratitis (vaccinia serpiginous ulcer). The phenomenon is probably due to the leucocytes penetrating the easiest into the cornea along the nerves

The impaired sensitivity in dendritic keratitis is in *Reiser's* opinion due to oedema especially in the limbal region whereas there is found no proper neuritis in the cornea

Gruter (quoted by *Severin* and *Reiser*) however claims to have observed inflammation of corneal nerves at an early stage of the disease by means of a special staining technique methylene blue. Further *Nakajima* (quoted by *Reiser*) found irregular thickening of brain stems in the cornea on examination in the slit lamp

If *Reiser's* theory is correct the corneal hypaesthesia should be rather diffusely extended over the whole cornea. *Holwich* stated in fact that the sensitivity was reduced throughout the cornea the impairment being not limited to the dendritic process. *Boberg-Aus* and *Severin* on the other hand noticed a more or less localized impairment of sensitivity

According to *Reiser's* theory normalisation of the sensitivity should be expected gradually as the disease improves and the oedema subsides

In agreement with this *Sood* found improvement of the sensitivity in the few cases of dendritic keratitis subjected to follow up examination with a cotton wisp

Severin however using *Cochet & Bonnet's* sensibilometer saw no improvement in the patients whose disease was located under Bowman's membrane. *Severin* is accordingly of the opinion that the disease is concentrated primarily in the corneal nerves and depends on the neurovirulence of the herpes virus

The corneal sensitivity seems to be of prognostic value. The more impaired it is the greater is the chance of recurrence (*Paton Simkova* (quoted by *Severin*) *Severin*)

Various unclarified questions are thus attached to the corneal sensitivity after dendritic keratitis. How often is the sensitivity impaired after dendritic keratitis? Does the sensitivity improve after many years or is the impairment stationary? Is the impaired sensitivity mainly diffuse or localized?

An attempt has been made to answer these questions by a follow up of 107 patients. The composition of the series as well as the observation period recur

rence rate incidence of corneal opacity blood vessel invasion Hudson Stahl's line visual impairment vital staining of the cornea and Fischer Schweitzer's fluorescein pattern have been dealt with in three previous papers (Norm 1969)

Method

Measurement of the corneal sensitivity with a nylon thread of variable length was introduced by *Boberg Ans*

Cochet & Bonnet's sensibilometer was used for the present study A nylon thread is passed so as to touch the cornea at right angles to this The thread may be varied in length so that the pressure applied against the cornea may range from 11 mg/0.0113 mm² to 200 mg/0.0113 mm²

The measurements are performed with the patient sitting on a chair and fixing a point above eye height There is a fairly strong light on the cornea allowing one to see exactly which point of this is touched and to control at which moment the thread touches the cornea and therefore becomes slightly curved

A curving of less than 5° is aimed at (*Cochet & Bonnet*)

One starts with maximum thread length corresponding to the lowest pressure (11 mg) and thereafter reduces the thread length at the following touches until the length at which the patient is just able to feel the touching The thread length is read and converted into mg/0.0113 mm² by the aid of the table supplied by the firm

The apparatus used can only measure values within the range of 11 to 200 mg/0.0113 mm² This means that an extremely high corneal sensitivity is recorded as 11 mg while asensitivity and a very pronounced hyposensitivity are recorded as 200 mg at most i.e. less than the true value

The applications are performed at a slow rate to avoid summational effect In the present series measurement was made first at the centre of the cornea and then at different points in the periphery attention having been concentrated on perimetering a possible localized hyposensitive region

If the assessments were unreliable the measurements were repeated some times

The contralateral eye was examined in the same manner

Result

The mean result of the sensitivity measurements at the centre of the cornea is shown in Table 1 The sensitivity was greatly impaired in the eye which had been affected with dendritic keratitis

Table I

Mean corneal sensitivity centrally on the cornea in 107 patients with previous dendritic keratitis measured with Cochet & Bonnet's aesthesiometer expressed in mg 0.0113 mm² (Thread diameter 0.12 mm)

	No of corneae	sensitivity	
		kerat aff eye	contralat. eye
unilateral	96	83	19
bilateral	22	49	-
Total	118	17	19

The weight on the cornea required for the touching to be recognized was on an average four times that on the cornea of the contralateral eye

By way of comparison it may be mentioned that *Cochet & Bonnet* take a difference in sensitivity exceeding 20-30% between the right and the left eye of a patient to be pathological

The investigation comprised 118 corneae from 96 patients 11 patients having had bilateral dendritic keratitis

In 81 per cent of the 96 unilateral cases a marked difference (over 30%) was found between the two eyes with impaired sensitivity of the keratitis affected eye Unlike in the control eye a minimum weight of 5 mg or more was required in this eye before the touching was recognized (5-10 mg in 17 per cent 11-24 mg in 1 per cent 25-51 mg in 11 per cent 52-64 mg in 15 per cent 65-134 mg in 26 per cent and more than 134 mg in 11 per cent)

In 4 per cent the difference between the two eyes was doubtful being less than 5 mg In 13 per cent the two corneae were equally sensitive and in 2 per cent hypaesthesia was found in the contralateral eye

In one of the two cases with sensitivity findings contrasting with those to be expected the measurement of the keratitis affected eye gave 75 mg and that of the contralateral eye 145 The latter eye presented a thick elevated bandular degeneration after injury which explains the impaired sensitivity

In the other case measurement gave 13 mg in the keratitis affected eye against 21 mg in the contralateral eye In this case no explanation could be given of the impaired sensitivity in the contralateral eye

The central corneal sensitivity of the contralateral eye averaged 19 mg By way of comparison it may be mentioned that *Cochet & Bonnet* using the same apparatus found it to average 11.6 mg in 112 normal eyes

The sensitivity was maximal i.e. measured at 11 mg in most cases of the present series. In 28 per cent it was impaired in 5 per cent even greatly so. In these latter cases a possible explanation could be given of the pronounced impairment: sequela of cataract extraction, iridocyclitis, corneal dystrophy, opacity of unknown cause and finally bandular corneal degeneration following injury seen in one case.

Site

Localized hypaesthesia was found in 48 per cent of 118 corneae.

The hypaesthesia was limited to the central region in 12 per cent. The sensitivity was often greatly impaired e.g. corresponding to 145 mg centrally against 21 mg at the inner periphery and 13 mg quite peripherally.

In 14 per cent the impaired sensitivity was limited to a peripheral fairly small often sector formed region. In the remaining 22 per cent about half of the cornea was particularly hypaesthetic.

In the other 57 per cent the corneal sensitivity was uniformly impaired or normal or it was mildly and uniformly impaired along the whole periphery compared with the central region as is seen in normals (Cochet & Bonnet).

If in the above statement (table I) the lowest sensitivity recorded independently of its site on the cornea had been employed instead of the value for the central part of the cornea a greater difference from the mean value for the control eye would have been found. It may however in some cases be difficult to decide whether a reduced sensitivity peripherally represents the normally occurring lower sensitivity in this region or whether it is due to a pathological process. On this account only the central value is counted.

Age and Sex

The report given below comprises only the 96 unilateral cases to render possible a direct comparison of the keratitis affected eye with the contralateral which acts as control.

Table II illustrates the dependence of the sensitivity on age. The sensitivity was seen to decrease markedly with increasing age both in the keratitis affected eye and in the control eye.

A similar fall has been described in normal series after the age of 40-50 (Boberg *Ans*). In the present series such a fall was perhaps seen from the age of 30. It was pronounced in the keratitis affected group where the age determined reduction of sensitivity was added to the pathologically impaired corneal sensitivity.

No significant sex difference was demonstrable.

Table II

Possible dependence of corneal sensitivity on age and sex in dendritic keratitis affected and in contralateral eye Sensitivity given in mg 0.0113 mm²

age	number	sensitivity	
		kerat aff eye	contralat eye
0-9	16	61	12
10-19	10	59	12
20-29	12	75	11
30-39	12	88	17
40-49	20	79	22
50-59	14	100	21
≥ 60	12	124	35
females	40	77	23
males	56	88	15
Total	96	83	19

Observation Period

The corneal sensitivity was measured in connection with a follow up of patients who had previously had dendritic keratitis

The first attack had occurred not less than 5 years – on an average 13 years – before the follow up

The patients who had had only one attack have been collected in table III

The impaired sensitivity in the keratitis affected eye seemed to be independent of the length of the observation period Especially no improvement of the sensitivity was seen in cases with a particularly long observation period

Recurrence

Patients who had had many relapses showed a strikingly low corneal sensitivity whereas patients with only few relapses had a better sensitivity (fig 1)

The contralateral eye on the other hand showed no correlation between sensitivity and recurrence rate

Two explanations may be offered of the observed correlation between impairment of sensitivity and recurrence rate in the keratitis affected eye Either patients with a greatly impaired sensitivity at the first attack are liable to repeated relapses (cf Severin) or the sensitivity becomes increasingly impaired after each new attack

Table III
 Corneal sensitivity compared with observation period in years 43 cases of dendritic keratitis without recurrence.

Obs period	number	corneal sensitivity (mg/0.0113 mm ²)	
		kerat. aff eye	contralat eye
< 6 yrs	14	64	14
7-8 yrs	9	39	11
9-10 yrs	10	61	15
11-12 yrs	7	63	30
13-18 yrs	9	106	11
> 18 yrs	1	900	11

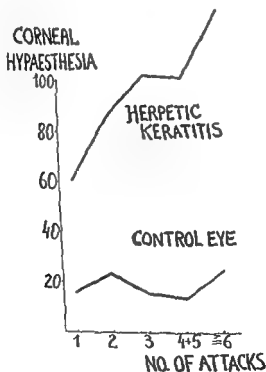


Fig 1

Correlation between number of attacks of dendritic keratitis and impairment of corneal sensitivity

Abscissa number of attacks

Ordinate mean corneal sensitivity expressed in mg/0.0113 mm²

Upper curve keratitis affected eye lower curve contralateral eye

Corneal Opacity

The sensitivity was most impaired in the cases showing corneal opacity. Note however that the sensitivity also was impaired in the group presenting no opacity (table IV).

The impairment seemed to be the greatest in the cases where the opacity extended the deepest into the parenchyma (table IV). On the other hand no definite correlation was demonstrable between the opaque area and the impairment of sensitivity.

The impairment was most pronounced in cases with blood vessel invasion of the cornea (on an average 108 mg in 50 patients with vascularisation against 56 mg in 46 without).

No correlation was noticed between presence of Hudson Stahl's pigment line in the cornea and impaired sensitivity (82 mg in 50 patients with the line and 84 mg in 46 patients without). This is surprising because Stahl's line is a very frequent phenomenon after dendritic keratitis (Norn 1969 B).

The cases classified in the case records as metaherpetic showed less corneal sensitivity than the non metaherpetic (99 mg against 69 mg).

Precorneal Film and Epithelium

The impaired sensitivity was most pronounced in the cases where the corneal surface was of poor quality manifesting itself by vital staining of the epithelium with fluorescein or rose bengal (107 mg in the 35 stainable cases against 69 mg in the 61 non stainable).

The sensitivity was most impaired in the eyes having the lowest wetting time.

Table IV

Possible dependence of corneal sensitivity on depth of corneal opacity. 96 patients who had had unilateral dendritic keratitis.

depth of opacity	number	sensitivity	
		kerat aff eye	contralat eye
no opacity	15	33	12
superficial	31	73	14
< 1/4	23	83	25
< 1/2	5	134	15
< 3/4	5	141	27
> 3/4	17	113	24

of the precorneal film (110 mg in the cases with permanently dry holes : = wetting time = zero 99 mg at wetting times from 1 to 10 seconds and only 74 mg at wetting times exceeding 29 seconds)

The patients with a pathological Fischer Schweitzer's fluorescein pattern had the most impaired corneal sensitivity (90 mg in 76 patients with a pathological pattern against 58 mg in 20 with a normal pattern) cf. Vorn 1969 C

Vital staining discloses defects and degeneration of the corneal epithelium the wetting time depends presumably on the epithelial layer of fat and Fischer Schweitzer's fluorescein pattern reflects sequelae of a pathological process close to Bowman's membrane. We do not know for certain whether the phenomenon is connected with structures deep to or superficial to the membrane.

Signs of present or previous pathological conditions in these superficial corneal layers may thus be correlated to the degree of sensitivity impairment though a causal relationship is unlikely where the most superficial phenomena are concerned

Impaired corneal sensitivity was more pronounced among the patients with signs of previous iritis (125 mg in 28 patients) than among the patients without such (66 mg in 68 patients)

No correlation or perhaps rather a slight negative correlation was found between sensitivity impairment and previous or present affection with herpes of the lips (19 mg in 46 patients with herpes against 81 mg in 30 patients without)

Visual Acuity

Table V gives a survey of the visual acuity at the follow up in relation to the

Table V

Corneal sensitivity compared with visual acuity of keratitis affected eye at the follow up Sensitivity given in mg 0.0113 mm²

visual acuity	number	sensitivity	
		kerat aff eye	contralat. eye
< 6/36	9	154	27
< 6/18	10	116	27
< 6/9	27	92	20
< 6/6	16	87	13
≥ 6/6	34	50	15
Total	96	83	19

impairment of sensitivity. A positive correlation was seen between the impairment of vision and that of sensitivity. The poorer the vision, the more impaired was the sensitivity. The control eye showed a slight tendency in the same direction, however.

Therapy

The impairment of sensitivity might be conceived to depend on the therapy given.

The investigation showed no difference between the patients treated with 5-iodo 2-deoxyuridine (IDU) and those treated by iodine cauterisation (on an average 90 mg in the IDU treated and 87 mg in the iodine treated. Control eye 21 and 18 mg respectively).

Impaired corneal sensitivity was perhaps more pronounced among the patients treated with steroids (average 103 mg, control eye 23 mg).

Discussion

The method employed for measuring corneal sensitivity is probably the most accurate one existing (Boberg, Ans, Cochet & Bonnet). The objections may be raised to this method that it is subjective, that repeated examinations may give somewhat unequal results, and that the range of measurements with the apparatus used is limited to 11–200 mg/0.0113 mm. Hypersensitivity therefore cannot be recorded, and – what is a greater disadvantage in the present investigation – more pronounced hyphaesthesia than that corresponding to 200 mg and proper anaesthesia are both recorded as hyphaesthesia of 200 mg. This latter fact probably means that the difference between the keratitis-affected eye and the control eye is greater than the tables indicate.

Is the impaired sensitivity in dendritic keratitis due to neuritis caused by the herpes virus, or to a more diffuse cellular infiltration with oedema, as supposed by Reiser?

The impaired sensitivity was limited to a circumscribed area in 48 per cent of the present series. This area was sector formed in some cases, while in others about half of the cornea was hyphaesthetic. The localized character might be conceived to be caused by oedema, which is particularly pronounced peripherally.

In 12 per cent out of 118 corneae the hyphaesthesia was localized centrally.

This does not harmonize with the hypothesis of oedema which according to Reiser is most pronounced in the limbal region

According to Reiser's theory the corneal nerves may in some instances be injured secondarily but a permanent impairment of sensitivity must be exceptional

The present sensitivity investigation is based on a follow up We do not know the degree of sensitivity during the first attack nor at subsequent attacks or between these

The mean impairment of sensitivity seemed however to be independent of the observation period In other words the sensitivity seemed not to improve in the course of years

This fact militates against Reiser's theory The frequent and pronounced impairment of sensitivity noticed in the present series indicates a considerable action on the corneal nerves which is rather to be interpreted as a sequela of neuritis due to the herpes virus

The impaired corneal sensitivity has in this series been compared with various other parameters The impairment was found to be most pronounced in cases with concurrent corneal opacity especially deep opacity with blood vessel invasion with defects of the corneal epithelium and the precorneal film and with alterations round Bowman's membrane previous iritis grave visual impairment and increased liability to recurrence

It is difficult to see which of these factors are primary which secondary and which perhaps independent

The impaired corneal sensitivity is possibly to be regarded as a primary factor The first attack by a particularly neurotropic virus may give rise to dendritic keratitis with very pronounced hypaesthesia (cf Severin) After the first attack the hypaesthetic cornea is liable to relapses This explains why the final result after several relapses is a cornea with a deep opacity and blood vessel invasion a deficiently covering precorneal film a vulnerable epithelium with degenerate epithelial cells defect of Fischer-Schweitzer's fluorescein pattern and a poor vision

How often are sequelae of dendritic keratitis detectable? (table VI)

Corneal opacity was present in III of the 96 patients with one eye affected In five of the remaining 13 cases a pathological Fischer-Schweitzer's pattern was seen

Of the last ten patients seven had a pathological corneal sensitivity (21.75 mg in the keratitis affected against 11 mg in the control eye)

Only three patients had no detectable sequelae None of these experienced recurrence One recovered in less than 48 hours

The seven cases in which hyposensitivity was measured in one eye with no

impairment of sensitivity. A positive correlation was seen between the impairment of vision and that of sensitivity. The poorer the vision, the more impaired was the sensitivity. The control eye showed a slight tendency in the same direction, however.

Therapy

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peripherally being sector formed while in 22 per cent it comprised half of the cornea and in the remainder it was diffuse

Declining corneal sensitivity was found to be positively correlated to rising number of relapses presence of opacity blood vessel invasion of the cornea stainability of the cornea reduced wetting time defects or absence of Fischer Schweitzer fluorescein pattern previous iritis and increasing impairment of vision It is possibly correlated to increasing depth of corneal opacity

The corneal sensitivity seems not to be correlated to the length of the observation period nor to presence of Hudson Stahli's line, and hardly to herpes of the lip

Sequelae of dendritic keratitis (opacity pathological Fischer Schweitzer's fluorescein pattern impaired sensitivity) were not visible in three of the 96 corneae

References

- Boberg Ans Jern Om corneasensibiliteten med særlig henblik på kliniske undersøgel-
sesmetoder (with an english summary) Thesis pp 192 Copenhagen 1952
- Cochet P & R Bonnet L'esthériométrie cornéenne. Réalisation et intérêt pratique
Bull soc d'ophtalmologie France 54: 550 (1961)
- Gordon Dan M & David A Karnofsky Chemotherapy of herpes simplex keratitis
Am J Ophthal 55 229 234 (1963)
- Gundersen Trygve Herpes cornea. With special reference to its treatment with strong
solution of iodine Arch Ophthal 15 225 249 (1936)
- Hollwich Frit Einführung in die Augenheilkunde Thieme Stuttgart 1968
- Vorn M S Dendritic (herpetic) keratitis I Incidence Season Variation Recurrence
Rate Visual Impairment Therapy Acta Ophthal 48 91 107 (1970 A)
- Vorn M S Dendritic (herpetic) keratitis II Follow Up Examination of Corneal Opa-
city Acta Ophthal 48 214 26 (1970 B)
- Vorn M S Dendritic (herpetic) keratitis III Follow Up Examination of the Pre
corneal Film Fischer Schweitzer's Fluorescein Pattern and Vital Staining Acta
Ophthal 48 277 286 (1970 C)
- Seravin Maria Die Hornhautsensibilität bei herpetischer Keratitis klin. Monatsbl
Augenheilk 146 683 695 (1965)
- Sood V V & V J Morrison Superficial herpetic keratitis treated with 5 iodo 2 de
oxyuridine Brit J Ophthal 48 609 614 (1964)
- Thygeson P S J Kimura & M J Hogan Observations on herpetic keratitis and ke-
ratoconjunctivitis Arch of Ophthal 56 315 338 (1956)
- Reuer K A Durch welche histologischen Veränderungen mit die Sensibilitätsstörungen
der Hornhaut beim Herpes zu erklären? klin. Monatsbl Augenheilk 104 257 263
(1940)

Table VI
Sequelae of dendritic keratitis in per cent

corneal opacity	85
blood vessel invasion	50
Hudson Stahli's line	52
pathol Fischer Schweitzer's pattern	19
hyposensitivity	81
opacity and/or pathological Fischer Schweitzer	90
opacity and/or pathological Fischer Schweitzer and/or hyposensitivity	97
no sequelae	3

other pathological findings are interesting because such cases may cause differential diagnostic difficulties within neuro ophthalmology if a history of previous keratitis is not available

It is remarkable that no more than 3 per cent completely avoided recognizable sequelae of dendritic keratitis

The series under review is in some measure selected in as far as it exclusively comprised patients referred to an ophthalmic out patient clinic. However the thorough clinical examination must be supposed very frequently to disclose sequelae of dendritic keratitis even in a non selected series

The results of the present study bore out the theory that measurement of the corneal sensitivity gives information of prognostic value in dendritic keratitis

Summary

A series of 96 patients who had had their first attack of unilateral dendritic keratitis not less than 5 years previously — on an average 13 years previously — had their corneal sensitivity measured with a nylon thread according to Boberg-Ans using Cochet & Bonnet's apparatus

In 81 per cent the sensitivity was markedly impaired compared with that of the contralateral eye. The average pressure required for the touching to be recognized was four times higher on the keratitis affected eye than on the contralateral

In 12 per cent the hypaesthetic region was localized centrally in 14 per cent

subcapsular layer of both lenses. A striking silvery grey delicate and complete rosette formation of petals tracing the fine feathery architecture of radiating lens fibers was observed. Visual acuity was not affected. Three weeks after withdrawal of Floropryl the changes had completely disappeared.

Jones & Watson (1967) reported bilateral angle closure glaucoma in a 7 year old boy treated with 0.125% Phospholine Iodide for an accommodative convergent squint. The tension was quickly normalized by atropine ointment but isolated gonio synchia persisted.

The present paper will describe some side effects observed in a group of young persons with various types of accommodative convergent deviations who were subjected to Floropryl or Phospholine Iodide therapy.

Material and Methods

The material consisted of seven boys aged 4-12 years and eleven girls or young women aged 6-23 years. A young woman aged 19 was treated with 0.1% Floropryl twice daily for three months whereas the other 17 patients were treated with Phospholine Iodide as a rule twice daily and in the concentration of 0.06% for periods varying from two to eight months.

Before treatment was begun the lenses were examined under mydriasis with a slit lamp. During treatment the patients were examined as a rule once a month. At first the anterior segment of the eye was examined whereafter the pupil was dilated with 10% Neo synephrine and the lenses examined.

Seventeen of these 18 patients were re-examined 6-10 months after discontinuance of treatment using the procedure described above.

Results

1. *Lenticular changes* Transient lens clouding was observed in the following two cases.

Case 1 L.H. ♀ aged 19 and treated with 0.1% Floropryl twice daily O.U. Before therapy was started only a few solitary vacuoles were seen in the lenses. After three months of treatment bilateral lens changes resembling those described by Harrison (1960) were observed with the exception that they appeared in both the anterior and the posterior subcapsular region. There was a striking accentuation of the normal feathery architecture of the lens. In oblique illumination and high magnification the bundles of lens fibers appeared swollen and were like strings of pearls. In retroillumination the pearls were seen to consist of very small vacuoles of about equal size. Remarkably enough visual acuity was not reduced. There were also iris cysts bilaterally.

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SIDE EFFECTS FROM USE OF LONG-ACTING CHOLINESTERASE INHIBITORS IN YOUNG PERSONS

BY

UNO AXELSSON and KARL GÖSTA NYMAN

Long acting cholinesterase inhibitors such as di isopropyl fluorophosphate (Floropryl) and echothiophate (Phospholine Iodide) are widely employed not only in the treatment of glaucoma but also in the management of accommodative convergent deviations. In the latter case their use is intended to reduce by inducing ciliary spasm the need for central accommodation and thereby also the central convergence impulse.

In young persons the local application of long acting cholinesterase inhibitors is known to cause side effects. Special attention has been directed to the frequent appearance of iris cysts. These however are considered innocuous because they do not impair visual function and disappear when the treatment is discontinued. Neo synephrine administered simultaneously with long acting cholinesterase inhibitors has been reported to diminish cyst formation without reducing the effect on the ciliary muscle.

Long acting cholinesterase inhibitors given to glaucoma patients have been shown to initiate or precipitate cataract formation (cf Axelsson & Holmberg 1966, Axelsson 1969). So far only Harrison (1960) has reported the appearance of lens opacities in young persons on administration of these drugs. A 13 year old girl with accommodative esotropia who was treated with Floropryl 0.025% bilaterally, developed after three months of treatment changes in the anterior

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* Neo synephrine® = metaxedrine (Winthrop USA)

of the iris may develop. It is possible that this side effect might have been prevented if Neo synephrine had been administered simultaneously with Floropryl or Phospholine Iodide.

As previously mentioned, angle closure precipitated by Phospholine Iodide has been reported by Jones & Watson (1967). It is well known that administration of long acting cholinesterase inhibitors to glaucomatous eyes with narrow angles may cause angle closure and formation of anterior synechiae. This risk must, of course, be considered also in young persons with accommodative convergent deviations who are often hyperopic and have small eyes with shallow anterior chambers. In our series no signs of angle closure and rise in tension were observed. It is impossible to decide whether anterior synechiae developed as gonioscopy was not performed.

Many authors have reported good results when treating accommodative convergent deviations with long acting cholinesterase inhibitors and the side effects were considered negligible. Our material is too small to permit a statistical evaluation of the results of treatment. We can only state the clinical impression that the therapeutic effect from the orthoptic point of view was far from excellent. We question whether the side effects of these drugs can be considered negligible. It must be borne in mind that the patients treated are young and that at present it is impossible to know how their lenses and out flow systems will behave in later life. As long as these facts are not known we think that long acting cholinesterase inhibitors should be used with caution in young persons.

Summary

A group of 18 young persons with various types of accommodative convergent deviations and treated with Floropryl or Phospholine Iodide, was studied with regard to side effects. Transient lens clouding was observed in two cases which are described in detail. Iris cysts appeared in seven patients. On re examination 6-10 months after discontinuance of treatment iris cysts persisted in three patients and in two a patchy depigmentation of the pupillary border and the surrounding iris was observed.

References

- Isaacs L. Glaucoma, motic therapy and cataract. Studies on echothiophate (Phospholine Iodide) and paraoxon (Mintacol) with regard to cataractogenic effect. Acta Ophth 1969 Suppl 107.

At this stage the Floropryl medication was discontinued and the patient was examined two weeks later. The changes described had undoubtedly regressed but numerous vacuoles still persisted. On subsequent examinations a gradual regression was observed and two and a half months after withdrawal of Floropryl only a few solitary vacuoles were seen. This was also the case 10 months after withdrawal. On the latter occasion a small iris cyst persisted in the right eye.

Case 2 J T ♂ aged 6. Before treatment started both eyes displayed remnants of the pupillary membrane and less than ten solitary lenticular vacuoles. Six and a half months after institution of Phospholine Iodide 0.125% twice daily both eyes exhibited lens changes of the type described for Case 1 but less pronounced and limited to sectors of the lenses. Besides iris cysts were found bilaterally. The treatment was then changed to Phospholine Iodide 0.06% twice daily. One month later the changes had regressed but clusters of vacuoles were still present. As at this time an allergic dermatitis had developed which was associated with the treatment Phospholine Iodide was withdrawn. After another month less than ten vacuoles were observed bilaterally. This applied also on re-examination ten months later but iris cysts persisted in both eyes.

B Iris cysts. During treatment iris cysts were observed in seven cases. On re-examination 6-10 months after treatment was discontinued iris cysts remained in three patients. Two of these were Case 1 and 2 described above. In the third patient a boy aged 8 and treated with Phospholine Iodide 0.125% twice daily for seven months nine large iris cysts were observed bilaterally seven months after withdrawal of the drug. Between the cysts there was a pronounced depigmentation of the pupillary border and the surrounding iris. In a girl aged 6 and treated with Phospholine Iodide 0.06% twice daily for four months similar depigmentation but no cysts was seen eight months after cessation of the therapy.

C Other side effects. Two patients had periods of diarrhea which however did not necessitate discontinuance of treatment. Another patient suffered from disturbed sleep which disappeared when medication was stopped.

Signs of angle closure were not observed but it should be pointed out that in no case was gonioscopy performed.

Discussion

The most interesting observation in the present study is the transient lens clouding that occurred in two cases. In both these the changes observed seem to have been identical with those described by Harrison (1960). It is evident that the lenses of young persons are also affected by strong cholinesterase inhibitors but are capable of recovery.

It is also evident that iris cysts do not always disappear when treatment with long acting cholinesterase inhibitors is discontinued and that persistent damage

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GLAUCOMA SCREENING

1 Critical Evaluation Based on Routine Tonometry among Members of the Volunteer Donor Corps of the Island of Falster (Denmark)

BY

KNUD NØRSKOV

Within the past 15-20 years reports on employment of routine tonometry for tracing glaucoma have been published in practically all parts of the world.

The investigations available so far have been reviewed by *Leydhecker* (1960) *Ourgaud & Etienne* (1961) *Posner & Fogland* (1964) and recently by *Segal & Skwarczynska* (1967) in which latter publication especially the Eastern European studies are well represented and by *Pollack* (1968).

The investigations reported differ appreciably with regard to composition of population groups, the screening limits chosen, the diagnostic examinations employed and criteria for early establishment of the diagnosis. Nevertheless the various investigators arrived at fairly equal results, namely that the tracings revealed not previously recognized glaucoma in from 1.5 to 2 per cent of the subjects examined above the age of 40. These investigators worked with a glaucoma concept based on the chosen criteria of glaucoma but did not, as recently proposed by *Hollows & Graham* (1966), distinguish between ocular hypertension and glaucoma with loss of function.

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Author's address: Anemonesvej 10, 50 Gentofte, Denmark.

- Axelsson U & Holmberg A* The frequency of cataract after miotic therapy *Acta Ophth* 1966 *44* 421
- Harrison R* Bilateral lens opacities associated with use of di isopropyl fluorophosphate eyedrops *Am J Ophth* 1960 *50* 153
- Jones D E P & Watson D M* Angle closure glaucoma precipitated by the use of Phospholine Iodide for esotropia in a child *Brit J Ophth* 1967 *51* 783

The obligingness of both management and members of the donor corps and the enthusiasm with which the staff of the blood bank took on the extra work of screening also contributed essentially towards carrying through the project.

Originally we intended to trace glaucoma by means of applanation tonometry and ophthalmoscopy. As however the great majority of the donors expressed a desire to have the testing amplified so much as to constitute a regular eye examination we decided to aim at complying with this desire to the greatest possible extent, trying to solve the topical eye problems of the donors.

The population group chosen comprised 2304 donors listed on May 1 1962 as active members of the volunteer donor corps of Falster. The collection period was concluded on January 31 1963.

The recording revealed that 265 of the donors (11 per cent) did not live on Falster but on Lolland a neighbouring island. As in decency we had to offer examination to all the donors irrespective of residence we decided to keep and examine the donor corps as an entity even though this involved that we did not as originally aimed at get a section of the Falster population alone.

A review of the card index of the only ophthalmic medical practitioner showed that primary glaucoma had been recognized previously in two donors (a woman aged 50 and a man aged 51) while secondary glaucoma was observed in one donor. In agreement with this the prevalence of previously recognized primary glaucoma (simple) was 0.09% while that for donors aged over 40 was 0.16%. These cases of previously recognized glaucoma were ruled out from the present investigation.

The number of donors who had applanation tonometry carried through was reduced for different reasons. Thus 109 donors had resigned membership within the period of investigation while we did not succeed in offering examination to 21 donors.

Of the 2221 donors (94 per cent) invited to applanation tonometry 69 (3 per cent) refused.

Finally an acceptable applanation tonometry could not be carried through in 191 cases. The majority of these belonged to the youngest age groups. Males and females were fairly equally represented. Ophthalmoscopy showed normal conditions in all the donors of this group.

Table 1 illustrates the age and sex distribution of the 2031 donors (86.3 per cent of the original number of donor corps members) subjected to applanation tonometry. It is seen that only 1146 donors (56 per cent) were over 40 years of age and 32 over 65. The mean age was 41 years for both males and females.

The withdrawals of blood took place between 8 a.m. and 9 p.m. and 52 per cent of the donors were examined after 6 o'clock p.m. The tonometry was carried through before the blood withdrawal except in the cases of 64 donors (3 per cent) where examination after the withdrawal had to be accepted for the sake of unrestrained performance of the withdrawal.

Since this publication a number of the writers concerned have felt called upon to recommend glaucoma screening to the greatest possible extent by means of tonometry, also among persons who normally have no contact with an ophthalmologist

Others hold a more critical attitude towards the problem of glaucoma screening as seen for instance in various reviews from recent years (*Hunt 1966 Leopold 1967, Noak 1967, Pollack 1968*)

This criticism has in the first place concentrated on fundamental objections to the usefulness of tonometry for tracing glaucoma at an early stage. In addition, it has been concerned with the practical and financial problems arising in relation to accomplishment of routine tonometry

In an endeavour to obtain a balanced evaluation of the advantages and disadvantages of glaucoma screening among individuals with apparently normal eyes members of the volunteer donor corps of the Island of Falster have been subjected to routine tonometry, using an applanation tonometer

The series was collected in relation to a glaucoma tracing investigation carried out on Falster during the period 1960-1963

Present Material

In choosing a population group on Falster (46 662 inhabitants) which might constitute the basis of an evaluation of routine tonometry carried through on persons with apparently normal eyes it proved to be difficult to find a sufficiently large group fit to be examined as planned by a single examiner within a reasonable time. Another difficulty was that of confining the examinations of such a group to a single place which was necessary owing to the use of an applanation tonometer

On Falster the prophylactic mass radiography for tuberculosis often employed for simultaneous screenings thus had an organizing form which did not allow of this combination

Further the Island of Falster has no industrial firms large enough to permit the desired limitation of routine tonometry to a single firm

This was the reason why the blood donor corps of Falster was chosen for an investigation based on routine tonometry. A possibility was thereby afforded of contacting a relatively large and well organized section of the population of Falster and at the same time of carrying through the screening in one place namely the Central Hospital of Nykøbing Falster where all donor blood withdrawals and donor health examinations take place

Table 2
Age and sex distribution of donors with applanation tonometric values above the screening level

Age	males	females	total	%
15-24	2	2	4	21
25-34	5	3	8	19
35-44	8	6	14	22
45-54	7	5	12	22
55-64	5	9	14	61
≥ 65	1	2	3	(9.4)
Total	28	27	55	27
	29%	37%		

32 donors (16 per cent) had values recorded of 22 mm Hg or higher and only six (0.30 per cent) values of 25 mm Hg or higher. For donors aged over 40 (1146 donors) the number of donors with pressure values ≥ 20 mm Hg ≥ 22 mm Hg and ≥ 25 mm Hg was respectively 3.4 per cent (39 donors) 2.0 per cent (23 donors) and 0.44 per cent (5 donors).

Further Examinations

The control examinations of 55 donors comprised not only renewed applanation tonometry, ophthalmoscopy and determination of the central visual acuity but also visual field measurement, gonioscopy and water provocative test. On 6 donors diurnal tension curves were obtained and 11 donors had Priscoll provocative tests carried out.

The results of the further examinations of the 55 donors selected on the screening were as follows:

1. Control of intra ocular pressure. Six donors (nine eyes) had pressure values of 25 mm Hg or higher recorded.
2. Ophthalmoscopy. 54 donors had normal optic discs. One donor was seen to have a cupped disc suspicious of glaucoma in one eye.
3. Visual field measurements. These were carried out by campimetry. Using object size 6/000 no visual field defects were detected whereas with size

Table 1

Age and sex distribution of 2031 donors subjected to applanation tonometry

Age	males	females	total
15-24	111	83	194
25-34	264	150	414
35-44	424	201	625
45-54	348	190	538
55-64	140	88	228
≥ 65	18	14	32
Total	1305	726	2031

Screening Level

It was decided that applanation tonometry showing an intra ocular pressure of 20 mm Hg or higher in one or both eyes and a difference of 4 mm Hg or higher between the right and the left eye motivated further examination with a view to presence of glaucoma

Applanation tonometric Values Below the Screening Level

In 1976 donors applanation tonometry gave values below 20 mm Hg in both eyes with a difference of less than 4 mm Hg between the right and the left eye. Thus the tonometry aroused no suspicion of glaucoma in these donors. On ophthalmoscopy all the optic discs were characterized as normal

Applanation tonometric Values Above the Screening Level

55 donors (2.7 per cent) had an applanation tonometric value above the screening level measured in one or both eyes. The age and sex distribution is seen in table 2. An intra ocular pressure above the screening level was more frequently measured in women than in men (3.7 and 2.2 per cent respectively). Within the age groups from 18 to 54 years the donors with pressure values above the screening level constituted approximately 2 per cent. This percentage was considerably higher (6.1) for donors between the ages of 55 and 64.

Table 9
Age and sex distribution of donors with applanation tonometric values above the screening level

Age	males	females	total	%
15-24	2	2	4	21
25-34	5	3	8	19
35-44	8	6	14	22
45-54	7	5	12	22
55-64	5	9	14	61
≥ 65	1	2	3	(94)
Total	28	27	55	27
	22%	37%		

37 donors (16 per cent) had values recorded of 22 mm Hg or higher and only six (0.30 per cent) values of 25 mm Hg or higher. For donors aged over 40 (1146 donors) the number of donors with pressure values ≥ 20 mm Hg ≥ 22 mm Hg and ≥ 25 mm Hg was respectively 34 per cent (39 donors) 20 per cent (23 donors) and 14 per cent (5 donors).

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Table 2

Age and sex distribution of donors with applanation tonometric values above the screening level

Age	males	females	total	%
15-24	0	2	4	21
25-34	2	3	8	19
35-44	8	6	14	22
45-54	7	5	12	22
55-64	5	9	14	61
≥ 65	1	2	3	(9.4)
Total	23	27	55	27
	22%	57%		

32 donors (16 per cent) had values recorded of 22 mm Hg or higher and only six (0.30 per cent) values of 25 mm Hg or higher. For donors aged over 40 (1146 donors) the number of donors with pressure values ≥ 20 mm Hg ≥ 22 mm Hg and ≥ 25 mm Hg was respectively 3.4 per cent (39 donors), 2.0 per cent (23 donors) and 0.44 per cent (5 donors).

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3. Visual field measurements: These were carried out by campimetry. Using object size 6/2000 no visual field defects were detected whereas with size

2/2000 visual field defects were observed in two donors (three eyes). It was in all three eyes a question of incipient defects – barring of the blind spot. Ophthalmoscopy showed two of the eyes to have normal optic discs. In the third eye the visual field defect noticed occurred in the only eye with a glaucoma suspicious optic disc.

4 Gonioscopy. In all the donors subjected to further examination the chamber angle was characterized as open in principle.

5 Provocative tests

a Water provocative test. 54 donors (108 eyes) were subjected to this test. A rise of 8 mm Hg or higher was released in 14 eyes or in 13.0 per cent of the water provocative tests. A detailed account of the experience gained from the water provocative test in the present series of screening examinations has been given in a previous paper (Narskov 1967a).

b Prisol provocative test. No more than two donors were subjected to this test. A rise of 11 mm Hg or higher was released in one case. A detailed account of the usefulness of the prisol provocative test in the present series of screenings has been given in a previous report (Narskov 1966).

Simple Glaucoma

One or more of the following criteria were required for establishing a diagnosis of glaucoma: 1 Distinct peripheral cupping of the optic disc (not met with in the present study); 2 Reproducible glaucomatous visual field defects; 3 Intraocular pressures of 25 mm Hg or higher; 4 A rise of 8 mm Hg or higher in response to water provocative test; 5 A rise of 11 mm Hg or higher in response to prisol provocative test.

On this basis a likely diagnosis of simple glaucoma was made in the cases of 20 eyes (12 donors) as shown in table 3.

The most frequent criterion was a pathological water provocative test (combined with pressures exceeding 20 mm Hg). Ophthalmoscopic findings were not employed and visual field defects occurred in three cases only. In three of the four cases in which the diagnosis was based on pressure measurements alone values of 30 mm Hg or higher were recorded.

Eight donors had the diagnosis made for both eyes and four donors for one eye only. The age and sex distribution is seen in table 4.

The incidence of glaucoma among all the donors was 0.59 per cent with no difference worth mentioning between females and males. None of the donors presented glaucoma at a fairly advanced stage. Thus only two (0.10 per cent) had small visual field defects: one in both eyes with no optic disc changes and the other in one eye where cupping of the optic disc was suspected.

Table 3

Criteria for establishment of a diagnosis of glaucoma in 20 eyes of 12 donors

1. Criteria present	4
pressure values ≥ 25 mm Hg	10
water provocative test ≥ 8 mm Hg	
2. Criteria present	1
pressure values ≥ 25 mm Hg + visual field defect	3
pressure values ≥ 25 mm Hg + water provocative test ≥ 8 mm Hg	1
priscot provocative test ≥ 11 mm Hg + visual field defect	
3. Criteria present	
pressure values ≥ 25 mm Hg + water provocative test	1
≥ 8 mm Hg + visual field defect	0

Table 4

Age and sex distribution of 12 donors with established diagnosis of glaucoma

Age	males	%	females	%	total	%
35-44	4	0.94	2	1.0	6	0.96
45-54	2	0.57	1	0.53	3	0.56
55-64	2	1.4	1	1.1	3	1.3
Total	8	0.61	4	0.55	12	0.57

Glaucoma was more frequent in the age group of 35-44 than in that of 45-54. Nevertheless only one donor - a woman aged 38 - had a diagnosis of glaucoma made before the age of 40. As might be expected the highest frequency of glaucoma was found in the age group of 55-64 (1.3 per cent) where as no donor over the age of 65 had glaucoma. For donors under the age of 40 the frequency of glaucoma was 0.11 per cent while for donors aged 40 or older it was 0.96 per cent.

In the present study the screening level was as stated set at 20 mm Hg. If a level of 21 mm Hg had been chosen instead the number of donors for further examinations would have been reduced from 55 to 43 whereas no influence on the number of newly diagnosed glaucoma cases would have been noticed. Setting the screening level at 23 mm Hg or higher further examination of 32 do-

nors (1.6 per cent) would have sufficed. However, in that case two donors corresponding to one sixth of the newly diagnosed glaucoma cases would have had no chance of getting their glaucoma disclosed by means of routine tonometry.

Normals

This group comprised donors for whom the results of all control examinations of both eyes were within the normal range, including pressure measurements below 20 mm Hg. No more than eight of the 55 donors selected on the screening could thus be said to have both eyes normal. This means that 14.5 per cent of the donors who on the screening had an applanation tonometric value of 20 mm Hg or higher recorded of one or both eyes could subsequently be registered as normal. The result of the screening must accordingly be characterized as false positive.

Borderline Cases

The borderline cases constituted the largest group among the donors subjected to further examination. In this group we could not establish a diagnosis of glaucoma nor refute a suspicion of this on the basis of the examinations performed and the criteria chosen for evidencing the glaucoma diagnosis and the normality concept employed (see above). The group comprised 35 donors (15 males and 20 females) of whom 32 presented bilateral anomalies.

The number of borderline cases constituted 1.7 per cent of the total number of donors subjected to routine tonometry.

Discussion

The results of the routine tonometries reported above showed in agreement with previous glaucoma screenings that tonometry may reveal not previously recognized glaucoma in persons with apparently normal eyes.

The frequency of glaucoma noted in the present study, where 1.59 per cent of all the donors examined and 0.96 per cent of those aged 40 or older had a diagnosis of glaucoma established, was lower than the usually stated 1.5 and

2 per cent for persons aged 40 or older. This difference is possibly due to pre dominance of the fairly young age classes in the population group under review and also to the fact that half of the donors had blood withdrawn after working hours having consequently been subjected to tonometry at a glaucoma prophylactically unfavourable time of the day.

However a review of Scandinavian reports on routine tonometry of persons with apparently normal eyes has shown that these examinations also gave a lower glaucoma frequency than the often stated 1.5 to 2 per cent for persons aged 40 or older (table 5).

In the three reports on tonometry of hospitalized patients the frequency was even 0.5 to 0.6 per cent. Possible explanations of the stated low frequency are discussed in a previous paper (Norstkov 1967b). Among these the well known fall of the intra ocular pressure during stay in hospital is pointed out.

To attain to a balanced evaluation of the glaucoma prophylactic contribution yielded by subjecting persons with apparently normal eyes to routine tonometry we must however compare the results achieved in the form of newly detected cases of glaucoma in its widest sense with the disadvantages noticed of carrying through a glaucoma screening based on tonometry.

In arranging a glaucoma tracing examination using tonometry among persons who normally have no contact with an ophthalmologist it must be rational from a social aspect to aim at associating the glaucoma screening with a prophylactic examination in progress (e.g. a campaign against tuberculosis) or concentrating the screening on other well organized population groups (in industrial plants, institutions or hospitals). This is to avoid construction of an independent organisation for prophylactic measures against a single eye disease.

The reported examination on the Island of Falster showed however that it may be difficult to carry through such an association without at the same time reducing the glaucoma prophylactic value of the examination. Thus the members of the Falster donor corps presented a - from a glaucoma prophylactic aspect - undesirable predominance of fairly young persons (44 per cent under 40) and only one third of the examined donors were women. A similar age and sex distribution has been observed in glaucoma screenings carried through at places of work (Leydhecker 1959, Dersik 1961, Pur 1964, Bertelsen et al 1965). In the cases of population examinations where routine tonometry is offered to a population aged 40 or older within a geographically well defined region a fairly small attendance among the elderly and the most exposed section of the population must likewise be accepted (Stromberg 1962, Hollows & Graham 1966).

In a coupling of this kind where as in the present study a large proportion of the donors (52 per cent) attended in the evening after working hours we must further accept a determination of the intra ocular pressure at an unfavourable time of the day from a glaucoma prophylactic aspect.

Table 5

Scandinavian routine tonometries among persons with apparently normal eyes outside the sphere of action of the ophthalmologist

	number	age	screening level (calibration table)	suspects	%	Glaucoma detected (previously unknown)			
						glaucomatous field loss	%	early glaucoma	%
Koskenoja & Orma (1955) (home for aged)	600	> 64	≥ 25 mm Hg (≤ 35/55) (1948)	83	13.8	-	-	-	15 2.5
Katavisto & Sammalkivi (1964)	5760	≥ 40	≥ 20.5 mm Hg (≤ 40/55) (1950)	391	6.8	-	-	-	24 0.5
(non ophthalmological in patients)									
Nerskov (1967)	314	≥ 35	≥ 20.5 mm Hg (≤ 40/55) (1955)	12	3.8	1	0.32	1	0.32
(non ophthalmological in patients)			≥ 20 mm Hg appl						2 0.64
Jensen (1968)	1051	> 40	≥ 22 mm Hg (≤ 35/55) (1955)	34	3.2	-	-	6	0.6
(non ophthalmological in patients)									6 0.6
Strumberg (1962)	7275	≥ 40	> 20.5 mm Hg (< 40/55) (1950)	325	4.5	11	0.15	-	-
(total population)									-
Bertelsen et al (1965)	1909	> 19	≥ 20.5 mm Hg (≤ 40/55) (1950)	144	7.5	3	0.16	12	0.6
(industrial workers)	(1108)	> 40							12 0.8
									12 1.4

The population is greatly interested in prophylactic examinations when such are offered in a well organized form. Thus for instance the offered tonometry was refused by less than 5 per cent of the donors concerned.

However the effectiveness of a glaucoma screening depends not only on the attendance at the primary screening but also on the extent to which suspects after the first screening really are prepared to submit to further examinations.

This seems to be a weak link of the glaucoma screening procedure as in glaucoma screenings where the glaucoma suspects are to apply to an ophthalmologist on their own initiative further examinations have been found difficult to carry through (Volpaw & Sherman 1954 Reed & Bendor Samuel 1957 Vaughan *et al* 1957 Power 1957 Lasky *et al* 1959 Mills 1959 Gray 1960 Bendor Samuel & May 1960 Garner & Dressler 1961 Taubenhans 1961 Radian *et al* 1963 Aehlig 1965 McDonald & Johnsons 1965 Bjornsson 1967).

The author arrived at the same result on routine tonometry in an ophthalmological practice. This was carried on concurrently with the investigation under review and showed that one third of the glaucoma suspects had to be summoned for re examination (Norskov to be published).

To attain to an acceptable solution of this problem a careful co ordination of the primary screening and the further examinations is required. According to the experience gained from the present investigation such a co ordination is only possible by adapting the additional examinations to the individual desires of the glaucoma suspects supplemented by intensive search for those who fail to appear. However a permanent solution on these lines is hardly possible without establishing special glaucoma clinics with the consequences such will involve.

Though from a theoretical aspect the applanation tonometer is regarded as the most accurate one of the clinically employed tonometers (Chandler 1965 Pollack 1961) this type was the tonometer of choice in only few of the screenings reported (Schmidt 1960 Harrison & Wolf 1964 Perkins 1965 Walker & Ladden 1966 Wright 1966 Hollows & Graham 1966 Norskov 1961b Bankes *et al* 1968).

In most of these investigations the tonometry was carried out by ophthalmologists which was also the case in the present study but trained technicians may probably very well be entrusted with performing applanation tonometry (Perkins 1965 Rosenthal 1961 Pollack 1967 Tonkin 1966).

Further it is possible with adequate assistance to carry through applanation tonometry as a screening at the same rate as indicated for Schiotz weight tonometer namely 20-25 persons per hour (Leydhecker 1961 Pollack 1968).

An applanation tonometer attached to the slit lamp has the disadvantage however of being expensive in first cost and difficult to transport. This may as is evident from the present investigation interfere with an unrestrained arrangement of routine tonometry.

	number	age	screening level (calibration table)	suspects	%	Glaucoma detected (previously unknown)					
						glaucomatous field loss	%	early glaucoma	%	total	%
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Jensen (1965) (non ophthalmological in patients)	1051	> 40	≥ 22 mm Hg (≤ 35/55) (1955)	34	3.2	-	-	6	0.6	6	0.6
Strömberg (1962) (total population)	7275	≥ 40	> 20.5 mm Hg ($< 40/55$) (1955)	325	4.5	11	0.15	-	-	-	-
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and thorough diagnosing there must be a limit to the number of examinations one can permit oneself to offer among other things because irrespective of the issues one might have difficulty in convincing the glaucoma suspects that they are not suffering from a rapidly vision endangering disease

There are also more fundamental causes of the great variations regarding the extents of the additional examinations

It is thus very inconvenient that we have no commonly accepted definition of early glaucoma, while at the same time as in the present investigation it is necessary to give an exact definition of early glaucoma by choosing definite pressure values and by selected provocative tests

Moreover the provocative tests are neither sufficiently sensitive nor sufficiently specific and in addition great uncertainty prevails as to whether these tests can foretell the chances of developing visual field defects in the individual eyes examined

The uncertainty prevailing regarding the definition of early glaucoma and the concept of normality involves that as a result of any routine tonometry we are left with a poorly defined group having pressures within the range of 20-24 mm Hg characterized as borderline cases In the present series this group was three times as large as that with an established glaucoma diagnosis

Opinions differ as to the chances that borderline cases may develop into manifest glaucoma In some of the screenings reported the chance has been considered to be so great that the borderline cases have been included in the calculated glaucoma frequency (e.g. Brav & Kirber 1951 Packer *et al* 1959 Dunbar & Goldberg 1960) Linner & Stromberg (1964 1967) on the other hand stated that persons with moderate ocular hypertension rarely develop manifest glaucoma

The group constituting the borderline cases is a deserted group within the glaucoma screening procedure These persons cannot be told that they are quite normal they are not to be treated but still to be under control The maintenance of the borderline cases must therefore also be considered when the total work to be performed as a result of glaucoma screening is to be evaluated

Among the new detected glaucoma cases disclosed by routine tonometry of persons with apparently normal eyes the form characterized as early glaucoma predominates as also seen in table 5 In the present study glaucomatous visual field defects were present in no more than 0.10 per cent corresponding to one sixth of the new detected glaucoma cases

The great majority of the cases disclosed by glaucoma screening being thus represented by glaucoma with absence of visual field defects it is evident that the prophylactic value of glaucoma screening depends largely on a knowledge of the further fates of these cases

It is remarkable that only two series are available so far which have been thoroughly examined with a view to assessing the further course in relation to

Regarding glaucoma screening among persons who have no contact with an ophthalmologist the primary screening by tonometry is intended to be carried out by the aid of other medical groups or trained technicians while the remaining part of the glaucoma prophylactic contribution rests with the ophthalmologist

The extra work thereby imposed on the ophthalmologist will depend on the number of persons suspected of glaucoma after the primary screening This number will be influenced by various factors such as the composition of the population group chosen systematic tonometer errors technical errors reading errors and the skill of the examiner The choice of screening level will also play a decisive role

Regarding choice of screening level it is however inconvenient that the lower limit of a harmful intra ocular pressure is not known for the individual eye It has therefore been necessary to define an upper normal limit on the basis of a statistical estimate of so called normal series The term ocular hypertension has been chosen for persons whose intra ocular pressure exceeds the mean value plus twice the standard deviation At the same time it has been tried to fix the screening level accordingly by routine tonometry

The trend is towards a lower screening level than previously and consequently an increased number of persons for further examination Thus a number of investigations have been published within recent years where using applanation tonometer and Schiotz weight tonometer a screening level of 20-21 mm Hg has been preferred (*Hunt 1966 Pollack 1968 see also table 5*)

The indications of pressure values above the screening level therefore also differ appreciably as seen in table 5 among others

The present investigation gave a frequency of 3.4 per cent for persons aged 40 or older Various other glaucoma screenings among normal population groups gave the result that more than 10 per cent of the persons examined at the primary screening were referable to further examination (*Brav & Kirber 1951 Wolpaw & Sherman 1974 Gradle & Downing 1957 Horsley et al 1958 Bankes et al 1968*)

At any rate to be able to disclose not previously recognized cases of glaucoma a considerable proportion of the persons with apparently normal eyes must be suspected after glaucoma screening

Further glaucoma screening in the normal population has the disadvantage that a group of persons is left to the care of an ophthalmologist who is expected to promptly make a diagnosis of glaucoma or acquit the examined of the suspicion

This practice has in fact been followed in most glaucoma screenings It means however that the grave diagnosis often as in the present investigation is made after a fairly limited number of examinations However even if one seems to have sufficient working capacity and enthusiasm enough for careful

and thorough diagnosing there must be a limit to the number of examinations one can permit oneself to offer among other things because irrespective of the issues one might have difficulty in convincing the glaucoma suspects that they are not suffering from a rapidly vision endangering disease

There are also more fundamental causes of the great variations regarding the extents of the additional examinations

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It is remarkable that only two series are available so far which have been thoroughly examined with a view to assessing the further course in relation to

glaucoma screening namely those of *Lanner & Strömberg* (1964 1967) and *Leydhecker* (1960 1966)

Unfortunately the conclusions arrived at are not identical *Leydhecker* is of the opinion that his results bore out the hypothesis that the rise in pressure precedes the visual field defects by 15-18 years a course which is a prerequisite of the prophylactic value of glaucoma screening *Lanner & Strömberg* on the other hand hold that glaucoma screening by tonometry is of no value from a glaucoma prophylactic aspect

In assessing the need for routine tonometry of the normal population the chances of contact with the ophthalmologist must also be considered In Denmark the geographical conditions as well as the structure of the health service afford possibilities of contact with an ophthalmologist In this connection it may be mentioned that 10 per cent of the present series of examined donors had consulted an ophthalmologist within a ten year period Further there is reason to point out that six of the 55 donors suspected to have glaucoma including the two with visual field defects also had been traced by a concurrent routine tonometry carried out by the only ophthalmic medical practitioner of Falster

These reflections offer nothing new However in many papers dealing with glaucoma tracing by tonometry the authors concerned have displayed a tendency towards underestimating the significance of the problems relating to a glaucoma prophylactic contribution based on tonometry The present investigation on the other hand has shown that glaucoma tracing examinations of persons with apparently normal eyes carried through on traditional lines may as often demonstrated disclose cases of not previously recognized glaucoma in its widest sense in 1.2 per cent of the population over 40 At the same time however the necessity has been stressed of a more critical view regarding employment of tonometry as an aid in the glaucoma prophylactic work This will in particular find expression in the attitude taken towards glaucoma screening outside the ordinary sphere of action of the ophthalmologists

Summary

The present investigation was carried through with a view to tracing glaucoma by means of applanation tonometry among 2031 persons 18 years old or older belonging to the volunteer donor corps of the Island of Falster (86 per cent of the total number of members)

In 55 donors (2.7 per cent) pressure values above the screening level (≥ 20 mm Hg) were recorded

One or more of the following criteria were required to establish the diagno

sis 1 Distinct marginal cupping of the disc (not observed in the present series)
 2 Reproducible glaucomatous visual field defects 3 Pressure measurements of
 95 mm Hg or higher 4 A rise of 8 mm Hg or higher in response to water
 provocative test and 5 a rise of 11 mm Hg or higher in response to prisol pro
 vocative test

After further examinations – including provocative tests – of the stated 55
 donors a diagnosis of glaucoma was evidenced in 0.59 per cent (12 donors,
 while for donors aged 40 or older the glaucoma frequency constituted 0.96 per
 cent. It was in no instance a question of glaucoma at a fairly advanced stage
 only two donors (0.10 per cent) having presented incipient visual field defects

Eight donors or 14.5 per cent of those subjected to further examination were
 characterized as normal or false positive all control examinations having given
 values within the normal range for both eyes including intra ocular pressures
 below 20 mm Hg

The borderline cases constituted 1.7 per cent (3 donors)

Starting from the experience gained from the present investigation various
 problems are discussed relating to the carrying through of glaucoma screening
 by means of tonometry. It is emphasized that on this basis we may be justified
 in a more critical view regarding employment of tonometry as an aid in the
 glaucoma prophylactic work. This will in particular find expression in the at
 titude taken towards glaucoma screening outside the ordinary sphere of action
 of the ophthalmologists

References

- Achlig A. Weitere ergebnisse der glaukom – reihenuntersuchung beim volksröntgen
 kataster. Klin. Wochenschr. 1965 146: 1-9
- Banks J. L. A. & S. Perkins S. Tsoulas & J. E. Wright. Bedford glaucoma survey
 Brit. med. J. 1963 1: 91-96
- Björdo Samuel J. & L. W. May & H. Reed. Routine tonometry in 5000 patients for
 detection of early glaucoma. Brit. med. J. 1960 1: 853-855
- Beitelstein T. M. Davanger. I. Kolstad L. Wirsching & H. Aasved. Maaling av det
 intraokulære trykk (Schiotz) og spaltelampeundersøkelse av personalet i en større
 bedrift. Tidsskr. norske Lægeforen. 1963 83: 449-453
- Björnsen C. The primary glaucoma in Iceland. Thesis. Acta Ophthalm. suppl. 91. Kbh.
 1966 p. 8-84
- Burton S. S. & H. P. Kirby. Mass screening for glaucoma. J. A. M. A. 1951 14: 112-114
- Candler P. A. & W. Morton Grant. Lectures on glaucoma. Philadelphia 1965 p. 33
- Dahl J. Detection of glaucoma in United States airforce personnel. Postgrad. Med.
 1961 30: 36-39
- Dunbar J. C. & M. C. Goldberg. Second glaucoma survey of Allegheny county and
 eastern Pennsylvania. Penn. med. J. 1960 63: 180-180c

- Garner L L & E Dressler G day in Milwaukee Sight sav Rev 1961 31 41 45
- Gradle A H & B Downing Community - wide glaucoma case finding Sight sav Rev 1957 27 78 82
- Gray R J Glaucoma survey of Pittsburgh and environs Penn. med J 1960 63 203 208
- Harrison R & E Wolf Glaucoma in elderly Amer J Ophthal 1964 57 236 241
- Hollows F C & P A Graham The Ferndale glaucoma survey In L B Hunt ed Glaucoma London 1966 p 24 44
- Horsley M E Ph Lewis & H Packer Glaucoma detection in an outpatient department J A M A 1958 166 1265 1269
- Hunt L B ed Glaucoma London 1966
- Jensen J Bruun Glaucoma screening with Schiotz tonometer and tensions indicator of applanation type Acta Ophthal 1968 46 638 642
- Kataavisto M & J Sammalvirta Tonometry among persons over 40 years of age Acta Ophthal 1964 42 370 377
- Koskenoja M & E Orma Routine tonometry for glaucoma detection in geriatric patients Geriatrics 1955 10 362 363
- Lasky M A L Zirmis & A Sands Glaucoma detection Amer J Ophthal 1959 48 515 516
- Leopold J H Glaucoma masque Editorial Amer J Ophthal 1967 63 174 179
- Leydhecker W Zur verbreitung des glaucoma simplex in der scheinbar gesunden augenärztlich nicht behandelten bevölkerung Docum Ophthal 1959 13 359 380
- Leydhecker W Glaukom - ein handbuch Berlin 1960 p 31 35
- Leydhecker W Die prognose des glaucoma simplex bei behandlung mit miotika im fruhstadium Klin Mbl Augenheilk 1960 137 606 612
- Leydhecker W Mass screening for glaucoma Amer J Ophthal 1961 51 248 253
- Leydhecker W Die zuverlässigkeit der diagnose des glaucoma simplex im fruhstadium Docum Ophthal 1966 20 214 229
- Linner E & U Stromberg The course of untreated ocular hypertension Acta Ophthal 1964 42 836 848
- Linner E & U Stromberg Ocular hypertension - a five year study of the total population in a Swedish town Skovde In Glaucoma symposium Tutzing Castle Basel 1967 p 187 194
- McDonald J E & M O Johnsons Glaucoma screening Amer J Ophthal 1963 59 815 883
- Mills G E Glaucoma screening in Connecticut Sight sav Rev 1959 29 144 148
- No ik R A Glaucoma screening - good or evil Eye Ear Nose Throat Monthly 1967 46 179 186
- Norskov A Priscot provocative test Acta Ophthal 1966 44 828 836
- Norskov A The water provocative test Acta Ophthal 1967a 45 57 61
- Norskov A Routine tonometry for detection of glaucoma in in patients with a five year follow up Acta Ophthal 1967b 45 536 545
- Norskov A Anvendelse af rutine tonometri i øjenpraksis To be published
- Ourgaud A G & E Étienne L exploration fonctionelle de l'oeil glaucomateux vol 1 Paris 1961 p 7 14
- Packer H & R Deutsch Ph M Lewis C D Oglesby & A C Chert Study of the frequency and distribution of glaucoma J A M A 1959 171 1090 1093
- Perkins E S Glaucoma screening from a public health clinic Brit med J 1965 1 417 419

- Pollack I P Diagnosis of the glaucomas In Symposium on glaucoma, Saint Louis 1961 p 31 37
- Pollack I P The challenge of glaucoma screening Surv Ophthal 1968 13 4 22
- Posner A & W G Fogland Mass screening for glaucoma a critical review of methods now in use Eye Ear Nose Throat Monthly 1964 43 53 60
- Power J L San Diego glaucoma survey Amer J Ophthal 1957 44 696 698
- Pur S k včasne diagnostice prosteho glaukomu Cs Oftal 1964 90 294 297
- Radian A II A L Radian M Iusev & N Jigau Organizarea si rezultatele unei actiuni de depistare precoce a glaucomului Oftalmologia Buc 1963 7 260 275
- Reed H & J E L Bender Samuel The detection of glaucoma before evidence of visual impairment Trans Ophthal Soc. II k. 1957 74 319 391
- Rosenthal J Evaluation of recall system for glaucoma suspects and patients Sight sav Rev 1967 37 18 87
- Schmidt Th Zur frubdiagnose und uberwachung des einfachen glaukoms Ophthalmologica 1960 139 260 2 11
- Segal P & J Skwierczynska Mass screening of adults for glaucoma Ophthalmologica 1967 153 336 348
- Stromberg U Ocular hypertension. Thesis Acta Ophthal suppl 69 kbh 1967
- Taubenhaus L J Glaucoma screening in Brookline Sight sav Rev 1961 31 18 22
- Tonkin II The early diagnosis of glaucoma Med J Aust 1966 2 1112 1115
- Vaughan D G R V Shaffer T Asbury S R Mettler W L Ridgway & R A Lot sprich Glaucoma detection in private practice and hospital Sight sav Rev 1957 145 148
- Walker W M & L M Vadden Birmingham glaucoma survey 1963 1965 In L B Hunt ed Glaucoma London 1966 p 4 11
- Wolpaw B J & A W Sherman The Cleveland glaucoma survey Sight sav Rev 1964 34 139 144
- Wright J E The Bedford glaucoma survey In L B Hunt ed Glaucoma London 1966 p 12 17

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GLAUCOMA SCREENING

II A Five-Year Follow-Up Carried Through in Relation to a Glaucoma Screening Among Members of the Volunteer Donor Corps of the Island of Falster (Denmark)

BY

KNUD NØRSKOV

Numerous glaucoma screenings using tonometry have been carried through within the past 15-20 years in attempts to add to the effectiveness of the glaucoma prophylactic work (Leydhecker 1960 Ourgaud & Ltienne 1961 Posner & Fogland 1964 Segal & Skwierczynska 1967 Pollack 1968)

To get conclusive evidence of the prophylactic value of examinations for tracing glaucoma it is however important to know the further course in the cases of persons subjected to glaucoma screening by means of tonometry. This is particularly important for the persons who have become suspected after glaucoma screening but as a matter of fact also for those characterized as normal after such screening.

It is therefore surprising that no more than two fairly large thoroughly examined series are available for assessing the further course in relation to glaucoma screening namely those published by Leydhecker (1960 1966) and Linner & Strömberg (1964 1967) with observation periods of 3 and 7 years and 1 3/4 and 5 years respectively.

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Leydhecker's results support the hypothesis advanced by Goldmann (1959) on the basis of Leydhecker's primary tracing among 10 000 persons (1959). According to this the ocular hypertension precedes the visual field defects by 15-18 years. This view was also recently borne out by Duke (1967).

Linner & Stromberg on the other hand arrived at a different result regarding the further course in the presence of ocular hypertension. They concluded that tracing of glaucoma by tonometry is of limited value as an aid to singling out persons who must be supposed later to develop manifest glaucoma.

Opinions thus differ considerably regarding the further course in the cases detected by routine tonometry and consequently regarding the prophylactic value of glaucoma screening.

On this background the results will be reported below of a five year follow up carried through in continuation of the original glaucoma screening by applanation tonometry among members of the volunteer donor corps on the Island of Falster.

The follow up comprised reexaminations and assessment of the course in the donors whose intra ocular pressure was measured at 20 mm Hg or higher at the primary screening. In addition the course was assessed in the donors characterized as normal after the primary screening on the basis of data obtained from the case records of the only ophthalmic medical practitioner of Falster.

Present Material

In a previous paper (Vorskov 1970) the results are reported of glaucoma screening using applanation tonometry among 2031 members aged 18 or older of the volunteer donor corps of Falster.

In 55 donors (2.7 per cent) an intra ocular pressure of 20 mm Hg or higher was then recorded. After further examinations a diagnosis of glaucoma (simple) was established in 12 donors while 30 were characterized as borderline cases and 8 as normal.

One or more of the following criteria were required to establish the diagnosis: 1. Distinct marginal cupping of the optic disc (which did not occur). 2. Reproducible visual field defects. 3. Intra ocular pressures of 20 mm Hg or higher. 4. A rise of 8 mm Hg or higher in response to water provocative test. 5. A rise of 11 mm Hg or higher in response to prisol provocative test. The normal group comprised the donors for whom all further examinations gave values within the normal range in both eyes including measurements below 20 mm Hg.

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Table 1

Age and sex distribution, and characterization of 52 donors included in the follow up

Age	glaucoma detected		borderline cases		normales		total	
	males	females	males	females	males	females	males	females
25-34	-	-	2	3	1	-	3	3
35-44	-	1	4	2	1	-	5	3
45-54	5	1	1	6	1	1	7	8
55-64	-	2	6	3	-	-	8	5
65-74	1	-	-	4	2	2	3	6
≥ 75	-	-	-	1	-	-	-	1
Total	8	4	13	19	5	3	26	26

showed the visual field to be normal in all 52 donors. Though repeated at tempts were made it was thus impossible to reproduce the visual field defect (barring of the blind spot) noticed previously in two donors (three eyes) though only with object size 2/2000. The observed discrepancy between the visual fields on the two examinations might therefore be due to the patient or the ophthalmologist having difficulty in recording when this object size was used. Note however that these two donors were both under treatment during the observation period a fact which may have influenced the appearance of the visual field.

Pressure level The pressure level during the observation period was estimated for all 52 donors (104 eyes) on the basis of measurements on the follow up examination supplemented by the measurements carried out by the ophthalmologist in the course of the five year observation period (table 2). 44 donors remained untreated. A level of 22 mm Hg or higher was recorded for 46 eyes corresponding to 44.2 per cent.

Among the 8 treated donors (5 from the glaucoma and 3 from the borderline group) only one obtained a reduction of the pressure to below 20 mm Hg while in 10 eyes the level was 22 mm Hg or higher. This evidences the difficulty not infrequently prevailing with regard to obtaining an ideal normalization of the intra ocular pressure in persons with ocular hypertension as pointed out by Walker (1976) among others.

In table 3 the pressure levels recorded for 44 untreated donors (88 eyes) on the ambulant control examination made in continuation of the screening have been set up against the levels found on the follow up examination after five

A Follow Up of the Donors with an Intra Ocular Pressure of 20 mm Hg or Higher on the Screening

The follow up examinations were carried out within the period from September 1967 to February 1968. Only 52 of the original 55 donors could be subjected to this examination. A woman aged 55 had died within the observation period and a man aged 71 failed to appear despite repeated written requests. Finally only three of the four donors who had left Falster within the observation period could be subjected to reexamination. The fourth, a man aged 31, was not examined. These three donors, who were not subjected to renewed control examination, had been characterized as borderline cases.

The follow up examination after five years of observation comprised estimation of the central visual acuity, ophthalmoscopy, visual field measurement and applanation tonometry. In compliance with the donor's desire, the times of examination were evenly distributed between 8 a.m. and 8 p.m. This was one of the reasons why the water provocative test was not repeated.

The ocular state of the individual donor was assessed on the basis of the results of these reexaminations, supplemented, if possible, by data available for the donors who had consulted the local ophthalmologist within the observation period.

20 donors, or 36 per cent, had consulted the ophthalmologist within the observation period. The number was considerably greater than the 16 per cent who had consulted the ophthalmologist within the group characterized as normal after the primary screening. Of the 12 donors who had had a diagnosis of glaucoma established, one third failed to appear for control (of the remaining 5 were treated). This is another evidence of the tendency, even among glaucoma patients, to remain absent from control, a factor which must be taken into consideration in assessing the prophylactic value of glaucoma screening (Muller & Glasenapp 1952, Wegener 1953, Leydhecker 1963, Joulers 1969, among others).

The age and sex distribution at the follow up of the 52 donors subjected to this reexamination is seen in table 1. The youngest donor was 25 and the oldest 76 years of age. The mean age was 51.6 (50.2 for males and 53.4 for females).

Results

Ophthalmoscopy Ophthalmoscopy revealed no changes in the appearance of the optic disc justifying a modification of the previous characterisation. In other words, both discs were still to be regarded as normal in 51 donors, while one donor had an unchanged glaucoma suspicious optic disc in one eye.

Visual field measurement Campimetry using object sizes 2/2000 and 6/2000

Table 1

Age and sex distribution, and characterization of 52 donors included in the follow up

Age	glaucoma detected		borderline cases		normales		total	
	males	females	males	females	males	females	males	females
25-34	-	-	2	3	1	-	3	3
35-44	-	1	4	2	1	-	5	3
45-54	5	1	1	6	1	1	7	8
55-64	2	2	6	3	-	-	8	5
65-74	1	-	-	4	2	2	3	6
≥ 75	-	-	-	1	-	-	-	1
Total	8	4	13	19	5	3	26	26

showed the visual field to be normal in all 52 donors. Though repeated at tempts were made it was thus impossible to reproduce the visual field defect (barring of the blind spot) noticed previously in two donors (three eyes) though only with object size 2/2000. The observed discrepancy between the visual fields on the two examinations might therefore be due to the patient or the ophthalmologist having difficulty in recording when this object size was used. Note however that these two donors were both under treatment during the observation period a fact which may have influenced the appearance of the visual field.

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Among the 8 treated donors (5 from the glaucoma and 3 from the borderline group) only one obtained a reduction of the pressure to below 20 mm Hg while in 10 eyes the level was 22 mm Hg or higher. This evidences the difficulty not infrequently prevailing with regard to obtaining an ideal normalization of the intra ocular pressure in persons with ocular hypertension as pointed out by Walker (1966) among others.

In table 3 the pressure levels recorded for 44 untreated donors (88 eyes) on the ambulant control examination made in continuation of the screening have been set up against the levels found on the follow up examination after five

Table 2
Pressure levels of 104 eyes (52 donors) during the observation period

	<20 mm Hg	20-21 mm Hg	22-24 mm Hg	≥25 mm Hg	total
No treatment	17	35	29	7	88
+ treatment	1	5	7	3	16
Total	18	40	36	10	104

Table 3
Comparison of the pressure level on primary ambulant control examination with that on five year follow up control examination in 88 eyes of 44 untreated donors

Primary ambulant control examination	follow up control examination			
	<20 mm Hg	20-21 mm Hg	22-24 mm Hg	≥25 mm Hg
< 20 mm Hg	14	7	-	-
20-21 mm Hg	-	23	12	1
22-24 mm Hg	3	5	11	3
≥ 25 mm Hg	-	3	4	2

years. In 50 eyes (56.8 per cent) the pressure had remained unchanged. In 15 eyes (17.0 per cent) a lower level was recorded at the follow up and in 23 eyes (26.1 per cent) a higher level.

As the values compared are based on single measurements which need not have been performed at the same time of the day the conclusions that we may be permitted to draw must necessarily be limited. It seems evident however that the pressure had not shifted exclusively to a higher level during the observation period. In only one donor was the intra ocular pressure seen to have risen to 25 mm Hg or higher in both eyes while a change from below 20 mm Hg to 25 mm Hg or higher never was recorded.

Similar shifts to both higher and lower pressure values in the individual cases have been recorded by *Lunner & Stromberg* (1964) as well as by *Leydhecker* (1966). This goes to show that the intra ocular pressure is not to be regarded as

a fixed value but is subject to variations. Consequently repeated pressure measurements may result in altered estimates in several cases.

Water provocative test At the primary screening 14 of the 108 eyes subjected to water provocative test (13.0 per cent) responded to this by a rise of 8 mm Hg or higher.

As stated above the water provocative test was not repeated.

However to evaluate the test we may look at the further course in the ten eyes which had a diagnosis of glaucoma established on a pathological water provocative test alone and which had remained untreated during the observation period. No more than three of these eyes showed a change of pressure to 25 mm Hg or higher.

Note that at the same time four donors (seven eyes) negative to water provocative test showed a rise of the intra ocular pressure to 25 mm Hg or higher at the follow up.

Our main impression of the results achieved is thus that the water provocative test seems to be of limited value as a basis for deciding in which cases the pressure will change during a five year observation period to a level that is harmful to the eye - in the present investigation set arbitrarily at 25 mm Hg.

In assessing the course during the observation period seen in relation to the chosen classification in glaucoma cases: borderline cases and normals we must bear in mind that a possible modification of the original characterization can be based on a change of the pressure level alone. None of the 52 donors followed up had developed ophthalmoscopically visible changes nor visual field changes and as stated above the water provocative test was not repeated. In conformity with the previously chosen criteria an intra ocular pressure below 20 mm Hg was characterized as normal while pressures ranging from 20 to 24 mm Hg were regarded as borderline values and 25 mm Hg or higher as glaucomatous levels.

Donors with an established diagnosis of glaucoma Table 1 shows the age and sex distribution at the time of the follow up for the 12 donors who had had a diagnosis of glaucoma established (in at least one eye). 4 donors were immediately subjected to antiglaucomatous treatment and one nine months later while 7 received no treatment (4 of them did not even appear for control).

It is seen in table 4 that despite intense antiglaucomatous treatment including strong miotics and diamox only one of the 5 treated donors obtained an ideal normalization i.e. below 20 mm Hg. One donor with a persisting intra ocular pressure of 25 mm Hg or higher despite drug treatment had both eyes subjected to antiglaucomatous operation. The table also shows that two thirds of the donors had a pressure level of 22 mm Hg or higher without ophthalmoscopy and visual field measurement having revealed development of glaucomatous changes.

As stated above no follow up record including water provocative test has

Table 4

Pressure level during the observation period in the cases of 12 donors (24 eyes) characterized as glaucoma cases

Pressure level	without treatment	+ treatment	total
< 20 mm Hg	—	1	1
20-21 mm Hg	5	2	7
22-24 mm Hg	6	4	10
≥ 25 mm Hg	3	3	6
Total	14	10	24

been carried through comparable to the previously performed further examinations. We therefore had no possibility of establishing the glaucoma diagnosis on the basis of the criteria set up at the follow up examination.

Donors characterized as borderline cases The age and sex distribution at the time of the follow up is shown in table 1 for the 32 donors characterized as borderline cases. As in other borderline cases no treatment was instituted after the conclusion of the further examinations. However, at a later stage of the observation period treatment was started of three donors of whom only two presented the criteria chosen in the present study for establishing the diagnosis of glaucoma.

In one of these a man aged 57 the pressure level had altered from 22-24 mm Hg to 26 mm Hg as the maximum value measured. The other was a woman aged 29 who after 18 months consulted the ophthalmologist — not to have her intra ocular pressure controlled as she had promised — but on account of conjunctival complaints. Measurement of the pressure gave 30 mm Hg in both eyes. During a subsequent stay in the ophthalmic unit pressure values up to 36 mm Hg were disclosed. Treatment with pilocarpine caused this donor such troubles that antiglaucomatous surgical intervention had to be carried through on both eyes.

It is seen in table 5 that pressure of 25 mm Hg and higher were recorded for four untreated eyes. In conformity with the chosen criteria of glaucoma the diagnosis must thus be regarded as established in both eyes of a woman aged 31 and a man aged 50. In both cases a rise was noticed from 22-24 mm Hg to 26 mm Hg as the maximum value measured.

A renewed assessment based on the course during the observation period of the conditions in the donors characterized as borderline cases gave the result that in four of the 32 donors a diagnosis of glaucoma must be regarded as

Table 3

Pressure level during the observation period in the cases of 32 donors (64 eyes) characterized as borderline cases

Pressure level	without treatment	+ treatment	total
< 20 mm Hg	3	-	3
20-21 mm Hg	28	3	31
22-24 mm Hg	23	3	26
≥ 25 mm Hg	4	-	4
Total	58	6	64

established according to the criteria chosen. As both ophthalmoscopy and visual field measurement showed normal conditions this altered classification was based solely on a change of the intra ocular pressure which even in three of these amounted to no more than a rise from 22-24 mm Hg to maximally 26 mm Hg recorded.

In one donor the characterization was on the given lines to be altered to normal.

Donors characterized as normal. In table 1 we see the age and sex distribution at the time of the follow up for the eight donors characterized as normal. In six the pressure level had remained unchanged below 20 mm Hg during the observation period. In the remaining two the pressure had risen to 20-21 mm Hg in one eye. These were therefore referred to the group of borderline cases according to the criteria employed.

B Follow Up of Donors Characterized as Normal on the Primary Screening

Few investigations have been made serving to assess the further fates of the persons characterized as normal after routine tonometry. Linner & Strömberg (1961) carried through a five year follow up of 639 persons born within the period 1895-1905. This number constituted 50 per cent of the persons of this age group whose intra ocular pressures had been measured at 40/55 Schiotz or lower at the primary screening in 1960 (Strömberg 1962). In the majority there was fair agreement between the results of the primary measurements and those of the measurements at the follow up. Only 25 (3.9 per cent) had an intra ocular pressure < 40/55 recorded without any influence on the ophthalmoscopic findings or visual field having been noticed.

In this connection there is also reason to mention the Des Moines population

study planned by *Armaly* (1960-1962) *Armaly* carried through a running pressure control of a population group though this is not to be regarded as a proper glaucoma screening

In a previous study (*Norskov* 1967) the author aimed at getting an impression of the further course in 301 patients who after routine tonometry during stay in hospital were characterized as normal judged from the data available from the case records of the only ophthalmic medical practitioner of Falster. None of the patients concerned had had a diagnosis of glaucoma established within the five year observation period.

Present Material

On the primary routine tonometry among members of the volunteer donor corps of Falster 1976 out of 2031 donors in 1962-1963 were characterized as normal (*Norskov* 1970).

A series of systematic control examinations for the purpose of assessing the course in this group was impossible to carry through. An attempt was made instead to get an impression of the further fates of these by utilizing the data available from the case records of the only ophthalmic medical practitioner of Falster.

A review of the case records from September 1967 to February 1968 revealed that within a five year period 307 (16 per cent) of the 1976 donors characterized as normal on the primary screening had consulted the ophthalmologist. Women predominated as is frequently seen in an ophthalmological practice (*Jensen* 1963, *Lorentzen* 1966) 22 per cent (151) being women and 12 per cent (156) men. Further the fairly old age classes were most richly represented. Thus while only 17 donors between the ages of 15 and 24 on the first examination had consulted the ophthalmologist the original age groups of 45-54 and 55-64 were represented by 101 donors (19 per cent) and 43 donors (20 per cent) respectively.

The patients were examined in accordance with the causes of their consulting the ophthalmologist. Ophthalmoscopy showed normal optic discs in all the cases. On the eye examination no point was made of a renewed recording of the intra ocular pressure. Therefore as seen in table 6 only 39 per cent (121 donors) had this measured. Among donors aged 45 or older the percentage was 47 per cent. However Table II also shows the age and sex distribution at the time of the follow up for the eight donors who had an intra ocular pressure of 20 mm Hg or higher recorded during the observation period. The frequencies of pressures of ≥ 20 mm Hg, ≥ 22 mm Hg and ≥ 25 mm Hg were 6.6% 3.3% (4 donors) and 0.33% (1 donor) respectively. The highest intra ocular pressure recorded was 25 mm Hg.

After the examinations comprising ophthalmoscopy, visual field measure

Table 6

Age and sex distribution of 121 previously normal donors who during the observation period had their intra ocular pressure recorded by the ophthalmologist

age	males	females	total	≥ 20 mm Hg	
				males	females
15-24	-	1	1	-	-
25-34	2	3	5	-	-
35-44	24	21	45	1	-
45-54	26	22	48	2	3
55-64	7	12	19	1	1
≥ 65	-	3	3	-	-
Total	50	62	121	4	4

ment and water provocative test (the latter employed systematically in cases only with a recorded pressure of 22 mm Hg or higher) a diagnosis of glaucoma based on the chosen criteria could be established in the case of one donor a man aged 48. The diagnosis was however based solely on pressures of 25 mm Hg or higher.

The data obtained from the only ophthalmic medical practitioner of Falster thus justified a diagnosis of glaucoma in one case though without loss of function within a five year period among the donors characterized as normal on the primary screening. We must bear in mind however that positive data were available for 307 donors only of whom no more than 39 per cent had their intra ocular pressure recorded.

The found frequency of pressures above the screening level cannot be regarded as representative of the whole donor group because these donors constituted an in a two fold sense selected section of the group. The donors concerned were to have consulted the ophthalmologist and he must have felt called upon to measure the intra ocular pressure.

These findings indicate however that a renewed pressure measurement after a five year observation period among persons characterized as normal on routine tonometry will disclose another series of pressures above the chosen screening level resulting in reflections regarding the necessity of control measurements and other additional examinations.

study planned by *Armaly* (1960, 1962) *Armaly* carried through a running pressure control of a population group though this is not to be regarded as a proper glaucoma screening

In a previous study (*Norskov* 1967) the author aimed at getting an impression of the further course in 301 patients who after routine tonometry during stay in hospital were characterized as normal judged from the data available from the case records of the only ophthalmic medical practitioner of Falster. None of the patients concerned had had a diagnosis of glaucoma established within the five year observation period

Present Material

On the primary routine tonometry among members of the volunteer donor corps of Falster 1976 out of 2031 donors in 1962-1963 were characterized as normal (*Norskov* 1970)

A series of systematic control examinations for the purpose of assessing the course in this group was impossible to carry through. An attempt was made instead to get an impression of the further fates of these by utilizing the data available from the case records of the only ophthalmic medical practitioner of Falster

A review of the case records from September 1967 to February 1968 revealed that within a five year period 307 (16 per cent) of the 1976 donors characterized as normal on the primary screening had consulted the ophthalmologist. Women predominated as is frequently seen in an ophthalmological practice (*Jensen* 1963, *Lorentzen* 1966) 22 per cent (151) being women and 12 per cent (156) men. Further the fairly old age classes were most richly represented. Thus while only 17 donors between the ages of 15 and 24 on the first examination had consulted the ophthalmologist the original age groups of 45-54 and 55-64 were represented by 101 donors (19 per cent) and 43 donors (20 per cent) respectively.

The patients were examined in accordance with the causes of their consulting the ophthalmologist. Ophthalmoscopy showed normal optic discs in all the cases. On the eye examination no point was made of a renewed recording of the intra ocular pressure. Therefore as seen in table 6 only 39 per cent (121 donors) had this measured. Among donors aged 45 or older the percentage was 47 per cent however. Table 6 also shows the age and sex distribution at the time of the follow up for the eight donors who had an intra ocular pressure of 20 mm Hg or higher recorded during the observation period. The frequencies of pressures of ≥ 20 mm Hg, ≥ 22 mm Hg and ≥ 25 mm Hg were 6.6% 3.3% (4 donors) and 0.83% (1 donor) respectively. The highest intra ocular pressure recorded was 25 mm Hg.

After the examinations comprising ophthalmoscopy, visual field measure

Table 6

Age and sex distribution of 121 previously normal donors who during the observation period had their intra ocular pressure recorded by the ophthalmologist

age	males	females	total	≥ 20 mm Hg	
				males	females
15-24	-	1	1	-	-
25-34	2	3	5	-	-
35-44	24	21	45	1	-
45-54	6	22	28	3	3
55-64	7	12	19	1	1
≥ 65	-	3	3	-	-
Total	59	62	121	4	4

ment and water provocative test (the latter employed systematically in cases only with a recorded pressure of 22 mm Hg or higher) a diagnosis of glaucoma based on the chosen criteria could be established in the case of one donor a man aged 48. The diagnosis was however based solely on pressures of 25 mm Hg or higher.

The data obtained from the only ophthalmic medical practitioner of Falster thus justified a diagnosis of glaucoma in one case though without loss of function, within a five year period among the donors characterized as normal on the primary screening. We must bear in mind however that positive data were available for 307 donors only of whom no more than 39 per cent had their intra ocular pressure recorded.

The found frequency of pressures above the screening level cannot be regarded as representative of the whole donor group because these donors constituted an in a two fold sense selected section of the group. The donors concerned were to have consulted the ophthalmologist and he must have felt called upon to measure the intra ocular pressure.

These findings indicate however that a renewed pressure measurement after a five year observation period among persons characterized as normal on routine tonometry will disclose another series of pressures above the chosen screening level resulting in reflections regarding the necessity of control measurements and other additional examinations.

Discussion and Conclusion

The object of the present investigation was in the first place to get an impression of the further course in a group with ocular hypertension disclosed by routine tonometry among persons with apparently normal eyes

A five year follow up comprising 52 donors (44 untreated) caught by routine tonometry the majority with pressures within the range of 20 to 25 mm Hg gave the results that no glaucomatous changes had occurred during the observation period neither of the visual field nor on ophthalmoscopy. Neither was any definite tendency towards a higher pressure level noticed.

To judge from the results of the present study the chance that a group of glaucoma suspects with no pathological changes of visual field or on ophthalmoscopy may develop such defects during a five year observation period must be regarded as fairly small. This is in agreement with Linner & Stromberg's experience from follow up examinations after 21 months which disclosed no glaucomatous defects on visual field measurement and ophthalmoscopy. On examination after five years of observation changes with regard to visual field ophthalmoscopic findings and pressure level were found in few cases only.

This view has also been borne out in more summary statements based on follow up examinations carried through by Bertelsen *et al* (1965) Fruhauf *et al* (1967), Norshov (1967) and Graham (1968).

As stated previously Leydhecker was of a different opinion regarding the further course in persons caught by glaucoma screening. On examination after three years of observation he found visual field defects developing in 32.5 per cent of those whose visual fields had previously been characterized as normal. Follow up examination after seven years of one fourth of the original number of glaucoma suspects revealed presence of visual field defects in 60 per cent of those with an intra ocular pressure of 22 mm Hg or higher.

In agreement with this Hildreth & Beeler (1957) in a group of glaucoma suspects detected by routine tonometry in an ophthalmic practice noticed that incipient visual field defects had developed in the course of 6.18 months in 39 per cent (49/69 persons) who originally had had a normal optic disc and visual field.

Leydhecker (1967) has pointed out as an explanation of the discrepant views regarding the further course in suspects caught by glaucoma screening that his series comprised pathological cases whereas Linner & Stromberg's series had pressure values at a high physiological level among other things because they had ruled out from their follow up persons with values within the range of $< 40/7.5$ Schiotz.

In the present investigation however the follow up comprised 94 per cent of the persons characterized as glaucoma suspects after the primary screening 44 per cent of these had pressure values of 22 mm Hg or higher during the ob

observation period while the primary screening had revealed incipient visual field defects in no more than two donors. This series thus represents the group predominating in all glaucoma tracing investigations in fact the group which gives occasion to many control examinations which are time wasting to both patient and ophthalmologist and also a strain on the nerves of the patient.

The situation is of course totally different for the fairly small group of patients displaying a fully developed (manifest) glaucoma with impaired functions at the glaucoma screening. These will have the same advantage of the disclosure of glaucoma as when the diagnosis is made by an ophthalmologist.

The classification employed on the primary glaucoma screening in glaucoma cases, borderline cases and normals has been preserved in the present investigation. This is the usual and also necessary procedure in screening. However the results of the follow up demonstrate the difficulty of maintaining such a classification. It might therefore be more appropriate in agreement with *Hollnagel & Graham* (1966) to use the term ocular hypertension for the whole group of glaucoma suspects detected on screening and reserve the term glaucoma for the cases presenting pathological glaucomatous changes on visual field measurement and ophthalmoscopy.

To be able to assess the glaucoma prophylactic value of glaucoma screening the further course in the cases with an intra ocular pressure below the screening level must also be considered. No direct comparison can be drawn between the five year control examinations carried through by *Linnér & Strömberg* of persons between the ages of 60 and 70 and the present investigation in which the assessment resulted from a retrospective study based on data regarding donors aged over 18 obtained from an ophthalmologist during a five year observation period. However in both groups pressure measurements at a follow up after five years of observation among persons characterized as normal on the original measurements revealed a new series of intra ocular pressures above the previously chosen screening level. None of these rises in pressure were associated with glaucomatous visual field defects or defects seen on ophthalmoscopy.

Linnér & Strömberg have drawn the conclusion that routine tonometry is of limited value as a means of disclosing the cases liable to develop into manifest glaucoma because the persons whose intra ocular pressure reaches a high level in the course of a five year observation period are recruited not only from the group with ocular hypertension but also from the group characterized as normal.

The question is however whether the whole glaucoma screening problem is not to be viewed from a different angle namely from the relation between the considerable number of persons caught by routine tonometry and the proper incidence of manifest glaucoma in the population.

Population examinations using tonometry will be of particular value to

throw some light on this question *Hollows & Graham* (1966) on a screening comprising persons between the ages of 40 and 75 found the incidence of simple glaucoma with associated pathological visual field defects and ophthalmoscopically visible changes to be 0.43 per cent. One third had been under ophthalmological control prior to the screening. A calculation based on Stromberg's screening of persons aged 40 or older gave an incidence of the same order (*Stromberg* 1962).

By way of comparison it may be mentioned that in a survey on Falster per October 1, 1960 before the commencement of the present series of routine tonometries the number of glaucoma cases diagnosed clinically by the only ophthalmic medical practitioner of the island amounted to 0.30 per cent (61 persons) of the population aged 40 or older (20 601 inhabitants aged 40 or older on Oct. 1 1960). Of these 0.23 per cent (48 persons) had simple glaucoma.

Among the members of the Falster donor corps aged 40 or older glaucoma had been diagnosed in two donors or 0.16 per cent before the routine tonometry.

In other words proper cases of manifest simple glaucoma are actually rarer than the usual statements based on glaucoma screening seem to suggest. This fact is a concurrent cause of the considerable difficulties prevailing with regard to getting a univocal estimate of the further course in the ocular hypertensive group disclosed by routine tonometry and thus regarding the assessment of the prophylactic value of glaucoma screening among persons with apparently normal eyes.

Finally the conclusion must be drawn that the results of the present investigation lend no support to our expectations regarding the prophylactic value of glaucoma screening but that at the same time continued follow up is desirable.

Summary

In the present paper the results are stated of a follow up carried through five years after a glaucoma screening by applanation tonometry of 2031 members of the volunteer donor corps of the Island of Falster. After the primary tracing 55 donors were suspected of having glaucoma. The diagnosis was established in 12 donors after control examinations and provocative tests on the basis of the criteria chosen while 35 donors were characterized as borderline cases and 8 as normal.

A follow up was carried through for 52 donors (between the ages of 25 and

16) the majority with intra ocular pressures ranging from 20 to 25 mm Hg 44 of these donors were untreated

It appeared that no glaucomatous changes were seen to have occurred during the five year observation period with regard to visual field and ophthalmoscopy Neither was a general change towards a higher pressure level observed

An assessment undertaken in relation to the classification in glaucoma cases, borderline cases and normals represented by 12 33 and 8 donors respectively gave the following results

None of the 12 donors with an established diagnosis of glaucoma of whom seven were untreated displayed any visual field defects after a five year observation period and only one slight cupping of the optic disc

In four out of 32 donors characterized as borderline cases the intra ocular pressure rose during the observation period to 25 mm Hg or higher justifying a diagnosis of glaucoma though without loss of function One donor was referable to the normal group after the follow up

Two of the eight donors originally characterized as normal were referable to the group of borderline cases after the follow up

An estimate of the course among the 1916 donors characterized as normal after the primary screening is based exclusively on data available from the only ophthalmic medical practitioner of Falster and comprises no more than 16 per cent of the total number Only one donor had a diagnosis of glaucoma established though without loss of function

The results of the present investigation have also disclosed the difficulties with regard to the arbitrary classification of glaucoma suspects usually employed in glaucoma screenings It therefore seems preferable to use the term ocular hypertension for the whole group of glaucoma suspects and reserve the term glaucoma for the cases with loss of function

Further possible explanations are given of the difficulties prevailing with regard to getting a univocal estimate of the further courses in persons caught by glaucoma screening

Finally the conclusion is drawn that the results of the present investigations lend no support to our expectations concerning the glaucoma prophylactic value of glaucoma screening but that at the same time continued follow up is desirable

References

- Armaly M F The Des Moines population study of glaucoma. Invest Ophthalmol 1967
1 618-68
Armaly M F A glaucoma survey J Iowa St. med Soc 1960 50 501-507

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- Segal P & I Skrzyszowska Mass screening of adults for glaucoma *Ophthalmologica* 1967 13 336 348
- Stromberg U Ocular hypertension Thesis *Acta Ophthalmol suppl* 69 Kbh 1962
- Walker W M Some problems in the medical treatment of glaucoma In L. B. Hunt ed *Glaucoma* London 1966 p 98 10
- Wegener W Gedanken zum glaukom *Klin. Mbl Augenheilk.* 1953 123 641 653

- Bertelsen T M Davanger A Kolstad L Wusching & H Aasved Måling av det intraoculære trykk (Schiotz) og spaltelampeundersøkelse av personalet i en større bedrift Tidsskr norske Lægeforen 1965 85 449 453
- Dake C L Glaucoma simplex - a long term clinical study Assen 1967 p 62
- Fruhauf A F Muller & M Sismuth Untersuchungen zur prognose des glaukoms Klin Mbl Augenheilk 1967 151 477 483
- Goldmann H Contribution to discussion on Leydhecker Zur verbreitung des glaucoma simplex in der scheinbar gesunden augenärztlich nicht behandelten bevölkerung Documenta Ophthal 1959 13 382 386
- Graham P Contribution to the ophthalmological Society of the United Kingdom 88 annual congress 1968 Brit J Ophthal 1968 52 64
- Hildreth H R & B Becker Routine tonometry Amer J Ophthal 1957 43 21 23
- Hollows F C & P A Graham The Ferndale glaucoma survey In L H Hunt ed Glaucoma London 1966 p 24 44
- Jensen O A Malignant melanomas of the uvea in Denmark 1943 1952 Thesis Acta Ophthal suppl 75 kbh 1963 p 65
- Jonkers G H Das glaukom als soziales problem Klin Mbl Augenheilk 1969 154 61 67
- Leydhecker W Zur verbreitung des glaucoma simplex in der scheinbar gesunden augenärztlich nicht behandelten bevölkerung Documenta Ophthal 1959 13 359 380
- Leydhecker W Glaukom - ein handbuch Berlin 1960 p 31 35
- Leydhecker W Die prognose des glaucoma simplex bei behandlung mit miotika im fruhstadium Klin Mbl Augenheilk 1960 137 606 612
- Leydhecker W Die entscheidung zwischen medikamentöser oder operativer therapie bei glaukom Klin Mbl Augenheilk 1963 142 260 266
- Leydhecker W Die zuverlässigkeit der diagnose des glaucoma simplex im fruhstadium Documenta Ophthal 1966 20 214 229
- Leydhecker W Contribution to discussion on Linner & Stromberg Ocular hypertension - a five year study of the total population in a swedish town Skovde In Glaucoma symposium Tutzing Castle Basel 1967 p 195 197
- Linner E & U Stromberg The course of untreated ocular hypertension Acta Ophthal 1964 42 836 848
- Linnér E & U Stromberg Ocular hypertension - a five year study of the total population in a swedish town Skovde In Glaucoma symposium Tutzing Castle Basel 1967 p 187 194
- Lorentsen S E Drusen of the optic disk Thesis Acta Ophthal suppl 90 kbh 1966 p 36
- Muller H A & I von Glasenapp Über erfahrungen bei der medikamentösen therapie des glaucoma simplex In P A Jaensch & R Thiel ed Glaukom Bucherei d augenärztes 21 heft 1952 Stuttgart 1952 p 81 100
- Nørskov K Routine tonometry for detection of glaucoma in in patients with a five year follow up Acta Ophthal 1967 45 536 545
- Nørskov K Glaucoma screening I Critical Evaluation Based on Routine Tonometry among Members of the Volunteer Donor Corps of the Island of Falster (Denmark) Acta Ophthal 1970 48 to be published
- Ourgaud A G & E Étienne L'exploration fonctionnelle de l'oeil glaucomateux vol 1 Paris 1961 p 7 14
- Pollack I P The challenge of glaucoma screening Surv Ophthal 1968 13 4 22
- Posner A & W G Fogland Mass screening for glaucoma a critical review of methods now in use Eye Ear Nose Throat Monthly 1964 43 53 61

Untersuchungsmethode

Der Stammbaum (Fig 1) wurde durch sechs Generationen unter Analyse von 86 Mitgliedern aufgezeichnet, 17 Mitglieder wurden von den Autoren unter Anwendung der Applanationstonometrie sowie Tonographie und Wasserbelastung untersucht. Alle wurde gonioskopiert und ophthalmoskopiert. Die Glaukomdiagnose wurde nach den von Tarkkanen (1962) angegebenen Kriterien gestellt. Die anamnestischen Daten wurden von einem Mitglied der Familie (III/27) gesammelt und kontrolliert. Dieses Mitglied war der Sohn eines Arztes II/13 mit verifiziertem Glaukom. Nach Möglichkeit wurde die Diagnose der erkrankten Familienmitglieder aus der Kartei des behandelnden Augenarztes kontrolliert. Im Ausland wohnhafte Mitglieder wurden von Augenärzten am Wohnort untersucht. Die Daten wurden den Autoren zu Verfügung gestellt.

Resultate

Der Stammvater der Familie (geboren 1808) war aus der Schweiz ausgewandert und starb im Alter von 57 Jahren. Eventuelle Augenkrankheiten sind nicht bekannt. Auch konnte über eventuelles Glaukom bei I/2 nicht Auskunft erhalten werden. Mitglieder der Familie der Frau I/2 leben heute noch und unter ihnen kommt Glaukom nicht vor. Der Stammvater scheint somit die Krankheit in seine Familie eingeführt zu haben. Die erkrankten Mitglieder in Generation

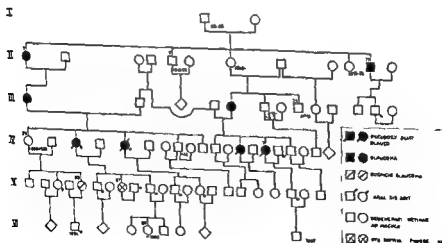


Fig 1

*Aus der Universitäts Augenklinik Helsinki
(Direktor Professor Salme Vannas)*

FAMILIARES VORKOMMEN VON PSEUDOEXFOLIATION UND GLAUKOM

VON

BIRGITTA KNAPE und CHRISTINA RAITTA

Familiäres Vorkommen von chronischem Weitwinkelglaukom ist seit langem bekannt. Die meisten Arbeiten befassen sich jedoch mit der juvenilen Form des Weitwinkelglaukoms, das entweder als ein verspätetes kongenitales Glaukom oder frühes seniles Glaukom aufgefasst werden kann. Die grosse Prävalenz des Simplexglaukoms in der Allgemeinbevölkerung machten das Deuten genetischer Untersuchungen oft schwierig. Dominanz, Pseudodominanz oder Rezessivität kann auch nur bei Untersuchung mehrerer als drei nacheinander folgenden Generationen bestimmt werden, da sonst die Möglichkeit der Kombination Homozygot und Heterozygot nicht ausgeschlossen werden kann. *Tarkkanen* (1962) und später *Tarllanen, Voipio & Korvusalo* (1965) befassten sich mit dem Erbgang bei Pseudoexfoliation und Glaukom. In vier Generationen fanden letzgenannte Autoren bei vier Mitgliedern Pseudoexfoliation, jedoch nur einmal kombiniert mit Glaukom.

Die Verfasser vorliegenden Artikels hatten Gelegenheit eine Familie durch 6 Generationen zu analysieren und Nachuntersuchungen an Mitgliedern 4 Generationen durchzuführen. Es wurde versucht, teils den Erbgang festzustellen, die zeitliche Reihenfolge Pseudoexfoliation – Drucksteigerung zu evaluieren sowie gleichzeitiges Vorkommen anderer Augenkrankheiten festzustellen.

Eingegangen am 2. September 1969

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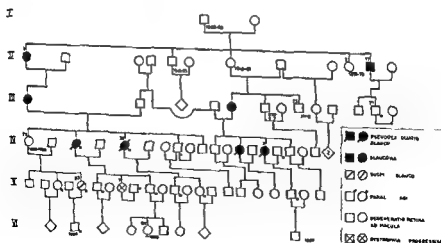


Fig 1

II und III hatten chronisches Glaukom über Abschlüpfung der Linsenkapsel sind keine Aufzeichnungen vorhanden Pseudoexfoliation kann nicht ausgeschlossen werden Die Mitglieder IV/31 IV/33, IV/41 und IV/43 haben alle ein Weitwinkelglaukom kombiniert mit Pseudoexfoliation Alle hatten bereits Gesichtsfelddefekte bei dem Stellen der Diagnose Das Alter der Patienten ist heute zwischen 70 und 75 Jahren Das Mitglied IV/29 ist mit 49 Jahren gestorben ohne das ein Glaukom diagnostiziert wurde Ihre Töchter V/53 ist das einzige Mitglied mit suspektem Glaukom und einem Druckniveau das zeitweise 30 mm Hg erreichte Abschlüpfung der Linsenkapsel wurde bis jetzt nicht beobachtet

Grosse Refraktionsanomalien fehlten in dieser Familie und ausser einer präsenilen und juvenilen Maculadegeneration V/52 VI/80 sowie dem Glaukom und der Pseudoexfoliation lagen keinerlei Augenerkrankungen vor Neurologische Erkrankungen wurden einmal in Form einer Paralysis agitans (VI/33 V/56) und einmal in Form einer Dystrophia musculorum progressiva diagnostiziert

Diskussion

Autosomale Dominanz war häufig der Erbgang bei Weitwinkelglaukom *Tarkkanen Voipio & Korvusalo* (1965) beschrieben eine Familie in der Pseudoexfoliation ausser mit Myopie und Glaukom auch für sich vorkam

In vorliegender Arbeit scheint sowohl Pseudoexfoliation als auch das Glaukom von einem Gen bestimmt zu sein Das Alter der Patienten bei dem sich die Krankheit manifestierte und der etwa gleichartige Verlauf waren charakteristisch Von besonderem Interesse ist das Mitglied V/53 eine Frau mit suspektem Glaukom aber einwandfreier Linse Durch Verfolgen des Verlaufes wird es vielleicht möglich festzustellen ob sich in dieser Familie das Glaukom vor der Pseudoexfoliation manifestiert

In Generation VI ist die Erkrankung wegen des Alters der Patienten noch nicht zu erwarten Es wurde gefolgert dass Pseudoexfoliation und Glaukom in verschiedenen Familien ein variables Vererbungsschema aufweisen kann Es ist somit klinisch wichtig den Typ festzustellen damit man die Frühdiagnosen stellen kann und auch eine adequate Therapie einrichten kann

Resultate

Ein Stammbaum mit 86 Mitgliedern durch 6 Generationen wurde aufgezogen Autosomale Dominanz von Pseudoexfoliation und Glaukom wurde festgestellt

stellt Das Alter der Erkrankten bei dem Manifestieren die Form der Krankheit schien gleichzeitig In keinem Fall wurde Pseudoexfoliation getrennt festgestellt und nur einmal suspektes Glaukom ohne Pseudoexfoliation

Literatur

- Tarkkanen A* Pseudoexfoliation of the lens capsule *Acta Ophth Suppl* 11 1962
Tarkkanen A Voipio H & Korvusalo P Family study of pseudoexfoliation and glaucoma *Acta Ophth* 43 619 633 1965

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Literatur

- Tarkkanen A* Pseudoxfoliation of the lens capsule *Acta Ophth Suppl* 71 1962
Tarkkanen A Voipio H & Korvivalo P Family study of pseudoxfoliation and glaucoma *Acta Ophth* 43 619 663 1965

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RECOGNITION OF THE LANDOLT RING AS A FUNCTION OF ITS ORIENTATION

BY

VIGO HEMMERSHØJ NIELSEN

Introduction

Differences in visual acuity as a function of different orientations of the test objects have been reported. Somewhat similar test objects were utilized in these investigations: Higgins & Stults (1,2) in 1948 and 1950 (parallel lines); Leibowitz (3) in 1953 (grating); Ogilvie & Taylor (4) in 1958 (fine wires); and Taylor (5) in 1963 (fine wires). All of the investigations show that a horizontal and vertical orientation of the test object yields a lower detection or recognition threshold than any other orientation. In all the studies the threshold for the horizontal and the vertical orientation are approximately identical.

Prince & Fry (6) (1958) have studied the problem of the orientation of the test object by using the Landolt Ring. Two emmetropic subjects were tested through a 3 millimeter artificial pupil and blurred by a +1.50 Diopter sphere. Their results point towards response differences between the four orientations and they present a formula which proposes to compensate for such response biases.

Procedure

Subsequent analysis of the data from a study by Nielsen (7) contains information about the recognition of a Landolt Ring as a function of four orientations.

Received October 10th 1969

The experimental conditions were identical for the four orientations and are summarized grossly* in the following points

- Black test object on white background (contrast ratio approaching $+1.0$)
- Large surrounding field
- Test field and surrounding field matched in brightness
- Uniform surface brightness (240 foot lambert)
- Exposure time of one second
- Monocular viewing
- Six observers and 2168 presentations

The experimental procedure was a four alternatives forced choice procedure and the Landolt Rings were presented in random order with the gaps oriented up down right and left. Each response was recorded as either right or wrong. The threshold was chosen to be at the $62\frac{1}{2}$ per cent correct response level.

Results

A frequency distribution of the visual angle thresholds for all orientations for the six observers is presented in Fig. 1.

Visual angle thresholds for each observer and each orientation is presented in the following table.

Table 1

Visual angle thresholds for each observer and averages for each orientation (visual angle of the outer diameter of the Landolt Ring)

	Up	Down	Right	Left	\bar{X}
I B	1.66	1.40	1.78	1.91	1.76
B F	1.89	1.72	2.37	2.26	2.06
M O	1.73	2.03	1.95	2.24	2.00
D S	1.96	2.05	1.81	2.03	1.93
F S	1.78	1.84	1.47	1.65	1.69
H T	1.96	2.19	1.87	1.98	2.00
\bar{X}	1.83	1.93	1.83	2.02	1.92

* A more elaborate description of the apparatus and procedure can be obtained from the author's M.S. thesis, Indiana University, Bloomington, Indiana, USA, May 1963.

The overall average visual angle threshold of the Landolt Ring (outer diameter) is 1.92 minutes of arc or 0.384 minutes of arc for the gap of the Landolt Ring. This is 23 seconds of arc which is in close agreement with Shlaer (8) (22 seconds of arc) and Schober (9) (24.5 seconds of arc).

A statistical analysis of variance was carried out to test a possible difference between the average visual angle thresholds of the four orientations but no statistical difference between them was found. A Chi Square test of variance was carried out for each observer to test individual differences but no statistical difference between the four orientations was found for any of the six observers.

Discussion and Conclusion

The frequency distribution of visual angle thresholds which is presented in Fig. 1 resembles the expected form of a psychometric response distribution. Replotted as per cent correct response as a function of increments in visual angle it resembles the familiar S shaped threshold curve.

The "up" and "right" orientations of the gap of the Landolt Ring yield average visual angle thresholds which are slightly lower than the overall average and the "down" and "left" orientations yield thresholds which are slightly higher. However the average visual angle threshold for any of the four orientations is within 0.1 minute of arc of the overall average.

The results of this study seem best interpreted as a confirmation of the findings from the majority of the cited studies. Namely that the orientation of an object or critical object detail in the horizontal and vertical meridian yield visual acuity thresholds which within minor differences statistically are the same.

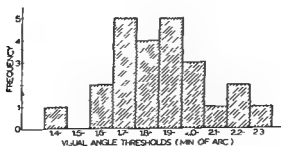


Fig. 1

Frequency distribution of the 24 visual angle thresholds based upon the outer diameter of the Landolt Ring.

Abstract

Under identical experimental conditions recognition thresholds have been determined for four orientations of the Landolt Ring (six observes and 2168 presentations). The results show that the differences (preferences) between the visual angle thresholds of the four orientations for each subject and for the four averages do not differ significantly.

Acknowledgment

This study was supported by a grant from A/S Fisker og Nielsens Fond Copenhagen Denmark for which the author wishes to express his gratitude.

References

- 1 Higgins G C & A Stultz Visual acuity as measured with various orientations of a parallel line test object, *Journal of the Optical Society of America* Vol 38 No 9 1948 756 758
- 2 Higgins G C & A Stult Variation of visual acuity with various test object orientations and viewing conditions *Journal of the Optical Society of America* Vol 40 No 3 1950 135 137
- 3 Leibowitz H Some observations and theory on the variation of visual acuity with the orientation of the test object *Journal of the Optical Society of America* Vol 43 No 10 1953 902 905
- 4 Ogilvie J C & M M Taylor Effect of orientation on the visibility of fine wires *Journal of the Optical Society of America* Vol 43 No 11 1953 628 629
- 5 Taylor M M Visual discrimination and orientation, *Journal of the Optical Society of America* Vol 53 No 6 1963 763 65
- 6 Prince J H & G A Fry Correction for the guessing bias in the Landolt Ring test *American Journal of Optometry and Arch of the American Academy of Optometry* Vol 35 134 141 1958
- 7 Nielsen V H Recognition of regular polygons in relation to visual acuity *American Journal of Optometry and Arch of the American Academy of Optometry* Vol 46 No 5 1969 378 356
- 8 Shlaer S The relation between visual acuity and illumination, *Journal of General Physiology* Vol 21 1957 16 158
- 9 Schober H & A Westmann Untersuchungen über die Sehschärfe bei verschieden farbigen Licht. (Quoted from Graham C. H. *Vision and Visual Perception* John Wiley and Sons Inc New York, London, Sydney 1965)
- 10 Schapero M H Cline & H W Hofstetter Editors *Dictionary of Visual Science* Chilton Company Philadelphia Pennsylvania 1960

Drammen Norway

60 YEARS RETROSPECT ON GLAUCOMA SIMPLEX

With special reference to Holth's iridencleisis

BY

HARALD G A GJESSING†

The author has passed through his case reports of all his 71 550 patients since he started as an ophthalmologist in Drammen South Norway in 1911 up to the summer 1969 1758 cases of simple glaucoma were found with a total of 2611 eyes suffering from that disease Only cases of simple glaucoma were included none of the other types e g narrow angle glaucoma glaucoma secundarium

There were three reasons for taking up this examination

- I Determination of the frequency of glaucoma simplex
- II To give an impression of the course of this disease treated medically or surgically
- III To evaluate the results of Holth's iridencleisis at a time when so many other operations are recommended

Many justified objections may arise against such a statement covering so long a period Neither can in a private practice so many examinations be performed as in the eye departments with their equipment and assistance Many simplifications have been necessary in the daily work for instance the water drinking test has only been used when the coffee test was questionable On the other hand all examinations and operations were performed by the same one man and evaluated by him

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Frequency

In the author's practice simple glaucoma occurred in 2.4% Ahlström mentioned 2% among 73 000 patients Malling and Thomas estimated a percentage of 8.4 based on a material in the University Eye Clinic of Oslo

1038 of the patients were males only 700 females In this the author's material differs from most others

In most of the 1758 cases the disease was monocular when first discovered During the observation period altogether 2671 eyes were found suffering from simple glaucoma The interval between the two eyes as a rule was several months to a few years

The course of simple glaucoma

For medical treatment was used pilocarpine 2.4% alone or with addition of eserine 0.5-1% With exception of Diamox administered systemically other drugs were seldom prescribed Mintacol was used in some few cases but never Phospholine jodide owing to the publications of Uno Axelsson and Per Riise of cataract induced by these drops

It appears that in 1405 cases the medical treatment kept the tension normal In 1717 the field of vision was found preserved by the last examination but shrunk more or less in 546 cases Visual acuity went down in 408 cases but the decline was seldom more than two lines of the usual Snellen test types

If we take the results by percentage of the three factors in glaucoma tension field of vision and visual acuity it appears that in about 80% the miotics had a good effect At least they could for a longer period delay the progression of the glaucoma

As the relevant indication for surgical intervention the author has always considered reduction of the field of vision in spite of medical treatment Prior to surgery medical treatment was used in an average of 50 months ranging from one to 3½ months Only when the patient at the first visit had shown himself undependable in using drops an operation was performed at once

Early operation might give a better prospect of a lasting result But also lasting amaurosis may follow surgery probably having relationship to an occurrence of the cavities of Schnabel But the author finds it a wise rule not to operate without proved loss of function

The author likes to emphasize that no operation for glaucoma gives an absolutely certain result even if it appears good immediately after the intervention This stands equally for the iridencleisis as for the other methods

Holth's iridencleisis operation

The good results obtained by the author's teacher S. Holth and his friend the Dane C. F. Bentzen induced the author to try the iridencleisis and since 1912 he has used it as the ordinary method. Holth's iridencleisis including meridional iridotomy has since been performed in 381 eyes, iridencleisis with peripheral iridectomy and iris inclusion in 14 eyes. Other methods were used in 151 eyes.

The operation was performed in Holth's original manner. The method was published in London 1939 with illustrations. Before that time the author had demonstrated the method in Vienna 1927 and in Birmingham, Sheffield, Manchester and York 1935. After these demonstrations the procedure was often called "the Norwegian method".

The results from the 381 performed Holth's iridencleisis operations might be summarized as follows: 308 (81%) normal tension, a few needing pilocarpine; 227 (60%) preserved visual field; 290 (71%) preserved visual acuity.

Even if some authors claim a higher percentage cured by iridencleisis the author thinks his results fairly good. The author's material is characterized by a special long observation time and during this might have developed macular degeneration, cataract and optic atrophy.

In this material the age of the patients seems to play a rather significant role. The prognosis was particularly bad for the youngest patients – whether treated by miotics or surgically. In the group from 60 years of age and upwards the prognosis was increasingly better.

Having performed 381 iridencleisis operations with meridional iridotomy and 14 with peripheral iris inclusion the author thinks himself justified to draw conclusions as to the value of the method.

One advantage is that Holth's operation gives a relatively thick covering of the fistula scar with a rather small risk of late infection. This holds true especially in the cases with meridional iridotomy. The risk of sympathetic ophthalmia is very small and never occurred in this material.

A second advantage is that with a well placed iridotomy a dazzling very seldom appears and also that – opposite to iridotaxis – the pupil is not drawn up.

A drawback of the iridencleisis is – opposed to the Elliot trephination – that the reduction of the intraocular pressure in about half of the cases is not achieved at once but only after some two to three months. During this time miotics are to be used. The patients are told to come back for reexamination. I am sorry not all have done so.

It may be added that the author never has seen hypotony after iridencleisis in his material whereas Christiansson had 11 cases of hypotony in 37 operations. The Seidel fistulation phenomenon very seldom occurred positive in the author's cases.

It must be rather unique that the same eye specialist for nearly sixty years has treated his cases of glaucoma simplex in the same manner in the same place and still does. His experiences may be of interest in a time when so many new drugs and operations are proposed.

Zusammenfassung

In einer augenärztlichen Praktik mit beinahe sechzigjähriger Tätigkeit befanden sich unter einem Krankengut von 71 550 Patienten 1758 Fälle von Glaucoma simplex (2,4%). 1058 waren Männer und 700 Frauen. Insgesamt 2671 Augen waren affiziert. In 1405 Fällen konnte medikamentöse Behandlung die Tension normalisieren. In 1212 blieben die Gesichtsfelder unverändert, in 546 Fällen waren sie eingeschränkt. 546 antiglaukomatöse Operationen wurden ausgeführt, davon 381 Iridencleissen mit meridionaler Iridotomie nach Holth, der vom Verfasser vorgezogene Eingriff. Die Resultate waren: Normalisierung der Tension in 81%, Konservierung des Gesichtsfeldes in 60% und Sehscharfe in 71%. Solange die Gesichtsfelder unverändert blieben, warnt der Verf. gegen Operation. Kein Fall von sympathischer Augenerkrankung kam vor. Die Normalisierung des Augendruckes nach Iridencleisis konnte sich zuweilen mehrere Monate verspaten.

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It may be added that the author never has seen hypotony after iridencleisis in his material, whereas Christiansson had 11 cases of hypotony in 37 operations. The Seidel fistulation phenomenon very seldom occurred positive in the author's cases.

Method and Material

In most cases ocular tension has been measured with a Schiøtz x tonometer. Some patients have been measured with a weighted Schiøtz tonometer only. A small number of patients in whom tension was measured only by means of an applanation tonometer have been omitted from this survey. Weighted tonometer readings have been converted in accordance with Schiøtz's 1924 calibration scale which we feel corresponds best to his original calibration scale for the x tonometer used for this material. According to this scale a reading of 35 with a 5.5 g plunger corresponds to an intraocular pressure of 27.5 mm Hg and a scale reading of 50 with a 7.5 g plunger to 29.5 mm Hg. To establish limits for glaucoma we have taken these readings as being equivalent to the scale reading of x/9 (= 28 mm Hg) on the x tonometer. The criteria for glaucoma applied are the same as those stated in our first survey (Acta Ophthal 46: 1095-1104) namely an ocular tension of x/9 or more if this can be confirmed by repeated measurements or if other symptoms of glaucoma are detected.

Our pseudoexfoliation material included only patients in whom pseudoexfoliation or glaucoma had not previously been observed. Out of an original total of 389 patients with unilateral pseudoexfoliation 343 were found suitable for comparison of ocular tension in both eyes namely 114 men and 229 women. Patients with traumatic influences of the eyes sequelae as a result of uveitis swollen cataract or other conditions which could be assumed to have an influence on the ocular tension have been omitted.

The frequency of glaucoma among patients in the material was 49.0% in respect of males (49 out of 114 patients) and 22.7% in respect of females (52 out of 229). In all these cases glaucoma was found in the eye with pseudoexfoliation. 7 men (6.1%) and 8 women (3.5%) also had glaucoma in the other eye.

Result

Figs 1 and 2 show the relative distribution of ocular tension in eyes with and without pseudoexfoliation. The curves show the relative distribution of tensions for the material as a whole i.e. including the glaucoma cases. The higher frequency of glaucoma in the men as opposed to the women is revealed by the fact that the curve representing eyes with pseudoexfoliation is more protracted in respect of the men than that of the women. The average figures for ocular tension in eyes without pseudoexfoliation are 20.4 mm Hg (S.D. = 3.82) and 19.0 mm Hg (S.D. = 3.41) for men and women respectively. It will be apparent that the dispersion is relatively slight. The average figures for tension in

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PSEUDOEXFOLIATION OF THE LENS CAPSULE

III Ocular tension in eyes with pseudoexfoliation

BY

EGILL HANSEN and OLE JAKOB SELLEVOLD

It has been well documented that pseudoexfoliation of the lens capsule frequently occurs in connection with glaucoma. Clinical experience has shown that in many cases even in patients who show no signs of glaucoma, there can be a higher level of tension in eyes with pseudoexfoliation than in eyes where no pseudoexfoliation is present. *Aasved* (1964) in connexion with his mass examination of elderly persons found that the ocular tension in patients with pseudoexfoliation was on an average 3 mm Hg higher than in the material taken as a whole.

In our material from Namdal Hospital (Acta Ophthal 46 1095 1104) we have been especially interested in comparing the tension in both eyes of patients with unilateral pseudoexfoliation. We believe that comparisons of this kind can provide useful information about the nature of the tension in eyes with pseudoexfoliation. Possible inaccuracies in the method of measuring employed will presumably apply equally as long as measurements are carried out in pairs and in the same way for both eyes in the same patient. Furthermore in the case of patients whom it has been possible to keep under observation over a protracted period of time we have attempted to register variability in the average tension level during the period of observation.

This investigation was partly supported by a grant from Dr Nils Helsingens Foundation for Medical Research at Namdal Hospital.

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Method and Material

In most cases ocular tension has been measured with a Schiøtz x tonometer. Some patients have been measured with a weighted Schiøtz tonometer only. A small number of patients in whom tension was measured only by means of an applanation tonometer have been omitted from this survey. Weighted tonometer readings have been converted in accordance with Schiøtz's 1924 calibration scale, which we feel corresponds best to his original calibration scale for the x tonometer used for this material. According to this scale a reading of 3.5 with a 5.5 g plunger corresponds to an intraocular pressure of 27.5 mm Hg and a scale reading of 5.5 with a 7.5 g plunger to 28.5 mm Hg. To establish limits for glaucoma we have taken these readings as being equivalent to the scale reading of x/9 (= 28 mm Hg) on the x tonometer. The criteria for glaucoma applied are the same as those stated in our first survey (Acta Ophthalm. 46: 1095-1104), namely an ocular tension of x/9 or more if this can be confirmed by repeated measurements or if other symptoms of glaucoma are detected.

Our pseudoexfoliation material included only patients in whom pseudoexfoliation or glaucoma had not previously been observed. Out of an original total of 389 patients with unilateral pseudoexfoliation 343 were found suitable for comparison of ocular tension in both eyes, namely 114 men and 229 women. Patients with traumatic influences of the eyes, sequelae as a result of uveitis, swollen cataract or other conditions which could be assumed to have an influence on the ocular tension have been omitted.

The frequency of glaucoma among patients in the material was 43.0% in respect of males (49 out of 114 patients) and 22.7% in respect of females (52 out of 229). In all these cases glaucoma was found in the eye with pseudoexfoliation. 7 men (6.1%) and 8 women (3.5%) also had glaucoma in the other eye.

Result

Figs 1 and 2 show the relative distribution of ocular tension in eyes with and without pseudoexfoliation. The curves show the relative distribution of tensions for the material as a whole, i.e. including the glaucoma cases. The higher frequency of glaucoma in the men as opposed to the women is revealed by the fact that the curve representing eyes with pseudoexfoliation is more protracted in respect of the men than that of the women. The average figures for ocular tension in eyes without pseudoexfoliation are 20.4 mm Hg (S.D. = 3.82) and 20.7 mm Hg (S.D. = 3.71) for men and women respectively. It will be apparent that the dispersion is relatively slight. The average figures for tension in

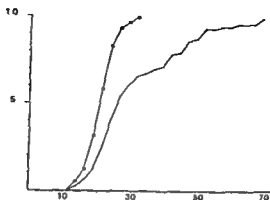


Fig 1

Cumulative polygons showing relative cumulative frequency of ocular tension in 114 men with unilateral pseudoexfoliation. The curve on the left shows the distribution of tension for eyes without pseudoexfoliation and the curve on the right that of eyes with pseudoexfoliation. The figures along the abscissa indicate the ocular tension in mm Hg and those along the ordinate the relative frequency.

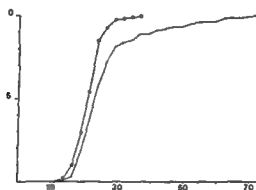


Fig 2

Cumulative polygons showing relative cumulative frequency of ocular tension in 279 women with unilateral pseudoexfoliation. Key to signatures as for Fig 1.

eyes with pseudoexfoliation is of little interest on account of the many instances of glaucoma in which the tension is considerably increased.

By leaving out all the patients with glaucoma we find the distribution of tension shown in Fig 3. The relative distribution of tension for eyes with and without pseudoexfoliation in 65 men and 177 women has been indicated on probability graph paper. There is a certain amount of deviation from normal distribution but this is not considerable. It will be seen that the tension curves run fairly parallel for both men and women. The tension curves in respect of

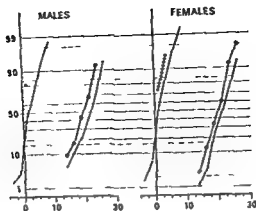


Fig 3

Cumulative polygons showing relative cumulative frequency of ocular tension in 65 men and 177 women with unilateral pseudoexfoliation without glaucoma. The curves marked with rings indicate the distribution of tension in respect of eyes without pseudoexfoliation while the unbroken lines indicate the distribution of tension in eyes with pseudoexfoliation.

The finely dotted curves show the relative cumulative distribution of deviations in tension between the eye with pseudoexfoliation and that without in the same patient. Also shown, for the sake of comparison is the relative cumulative distribution of deviations in tension in respect of the two eyes in 59 men and 88 women with bilateral pseudoexfoliation (square dotted curves).

The figures along the abscissa indicate the ocular tension in mm Hg and those along the ordinate the relative frequency.

the women lie closer together which is an indication of a lower average difference in tension in the women than in the men. The relative distribution of differences in tension is indicated on the far left of the diagrams. The curves which correspond best in the comparison between men and women are those in respect of the exfoliated eyes. The average ocular tension for eyes with pseudoexfoliation was 21.38 mm Hg in respect of men ($S.D. = 3.75$) and 21.41 mm Hg ($S.D. = 3.79$) in respect of women and for eyes without pseudoexfoliation 19.77 mm Hg ($S.D. = 3.44$) and 20.01 mm Hg ($S.D. = 3.15$) in respect of men and women respectively.

There is thus a marked difference in the level of tension in eyes with pseudoexfoliation compared to those without. The greatest difference in tension was 10 mm Hg. Also noted in some cases was a lower tension in the eye with pseudoexfoliation than in the other eye: 2 of the men (3.0%) and 11 of the women (6.2%) had a tension of at least 1.25 mm Hg lower in the eye with pseudoexfoliation than in the eye without. On an average however the ocular tension in the eye with pseudoexfoliation was 2.15 mm Hg higher than in the eye

without pseudoexfoliation in the case of men ($S D = 2.65$) and 1.46 mm Hg higher in the case of women ($S D = 2.41$). The corresponding t values are 6.56 and 8.04 for men and women respectively in other words the average difference in tension in both cases is significantly greater than 0 ($p = 0.01$).

Amongst the men 17 out of 65 had a clearly higher ocular tension in the eye with pseudoexfoliation than in the other eye namely a difference of 3.15 mm Hg or more whereas amongst the women 28 out of 177 had a positive difference in tension of 3.75 mm Hg or more in respect of the eye with pseudoexfoliation. The difference is not significant ($p = 0.05$). In other words no real difference can be shown between men and women in respect of the proportion of patients with a clearly higher tension in the eye with pseudoexfoliation.

The tension level in eyes with bilateral pseudoexfoliation

Amongst patients with bilateral pseudoexfoliation but without glaucoma in either eye we have made comparisons of the tension levels in both eyes. After setting aside all patients with sequelae as a result of uveitis likewise those whose eyes had suffered damage or been subjected to operations or in any way featured conditions which might exercise influence on the ocular tension we were left with 59 men and 88 women in whom the ocular tension in both eyes could be compared. Amongst the men the average ocular tension was 19.78 mm Hg ($S D = 3.37$) and amongst the women 20.94 mm Hg ($S D = 3.55$). There was an average difference in tension between the eye with the highest tension and the other eye of 0.53 mm Hg in respect of the men ($S D = 1.07$) and 0.78 mm Hg in respect of the women ($S D = 1.42$). The results are shown in Fig. 3 by means of the square dot curves. It will be seen that 81.3% of the men had a difference in tension of less than 1.25 mm Hg. In the case of the women 73.9% had differences in tension of less than 1.25 mm Hg and 95.5% had a difference of less than 3.75 mm Hg. Thus amongst our patients with bilateral pseudoexfoliation without glaucoma there is very little difference between the level of tension in the two eyes.

When comparing the difference in tension in the two eyes in patients with unilateral pseudoexfoliation and in those with bilateral pseudoexfoliation we found that in 30 out of 65 men with unilateral pseudoexfoliation the tension was at least 1.25 mm Hg higher in the eye with pseudoexfoliation than in the other eye. Among the men with bilateral pseudoexfoliation only 19 out of 59 showed a difference of at least 1.25 mm Hg between the eye with the highest tension and that with the lowest. The difference is very significant ($p = 0.01$).

As regards the women with unilateral pseudoexfoliation 82 out of 177 revealed a difference in tension of 1.25 mm Hg or more between the eye with pseudoexfoliation and that without whereas only 23 out of 88 in the group with bilateral pseudoexfoliation had a difference of tension of at least 1.25 mm

Hg between the two eyes. The difference is very significant ($p = 0.01$). Furthermore, 28 out of the group of 177 women had a positively higher tension in the eye with pseudoexfoliation of at least 3.75 mm Hg whereas only 4 of the women in the group of 88 with bilateral pseudoexfoliation had such a marked difference in tension between the two eyes. The difference is significant ($p = 0.05$).

Stability of the tension level during the period of observation

In order to determine whether the level of tension in eyes with pseudoexfoliation remains constant or whether there is a tendency for the tension to increase with time we kept a number of patients with pseudoexfoliation in one eye under observation and recorded the variations in tension in this eye from year to year. This group comprises patients who did not develop glaucoma and to whom moreover no glaucoma medication was administered.

Deviations from the initial tension were noted for each year of observation. In the case of patients in whom tension was measured several times in the course of a single year the deviation figure has been assessed as an average of these. By initial tension we mean the tension measured the first time pseudoexfoliation was observed in the patient in question. Table I shows the results in respect of 36 men and 73 women. The average initial tension in the men was 20.3 mm Hg (S.D. = 3.75) and in the women 20.7 mm Hg (S.D. = 2.97). The table indicates the average deviation from the initial tension for each year on the basis of the deviations registered for each individual patient. It will be seen that the deviations on an average are small over the period of observation as a whole. The degree of dispersion however is comparatively large as is revealed by the standard deviations. Thus no increase can be demonstrated in the average level of tension in eyes with pseudoexfoliation in these patients who have been kept under observation without developing glaucoma.

Comments

When pseudoexfoliation is first detected glaucoma is also observed in a considerable number of patients. In our total material of 736 patients in whom pseudoexfoliation had been recently discovered 45.5% of the men and 30.8% of the women had glaucoma (Acta Ophthal. 46: 1095-1104). Amongst patients who do not have glaucoma when pseudoexfoliation is first detected a number contract glaucoma in due course. At least 12 to 14% of the patients with unilateral pseudoexfoliation developed glaucoma in the course of a 5 year period.

Table 1
 Variations in the ocular tension in patients with unilateral pseudoexfoliation The figures indicate the average deviations from the initial tension calculated on the basis of observations recorded in respect of each individual patient The table refers to eyes with pseudoexfoliation

Year of observation		0-1	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9	9-10	> 10
Males												
No of patients		20	17	10	8	7	7	3	3	1	3	
Average deviation from initial tension		+ 0.5	- 0.5	+ 0.8	- 0.4	- 0.2	+ 0.3	0	- 1.7	0	- 0.3	
S D		2.85	2.61	4.13	3.33	3.34	3.81	3.00	1.53		3.51	
Females												
No of patients		30	34	29	22	18	12	7	5	3	3	1
Average deviation from initial tension		+ 0.5	- 1.1	- 0.3	+ 0.1	- 0.8	+ 0.3	- 0.9	- 0.3	- 3.2	- 3.2	- 2.3
S D		3.38	3.01	3.16	3.02	2.63	4.60	2.46	3.12	4.91	1.89	5.51

of observation whereas on the other hand at least 37 to 38 % were observed during the same period without developing glaucoma (Acta Ophthal 47 161-173) In other words in patients in whom pseudoexfoliation has been recently detected and glaucoma is not present from the outset the chances of developing glaucoma later on are not excessively great though they still exist Observation carried out over an even longer period confirms the same thing It is by no means unusual for patients to have had pseudoexfoliation for many years without any demonstrable damage being done to the eye In such cases the condition appears to become stabilized

In patients examined in the course of the present survey we find when conditions in the two eyes are comparable and glaucoma is not present that the average level of tension is significantly higher in the eyes with pseudoexfoliation compared with the level of tension in eyes in which pseudoexfoliation is not present In the patients with unilateral pseudoexfoliation who were kept under observation without developing glaucoma the tension in the eyes with pseudoexfoliation showed no tendency to increase even after a number of years The tension in these eyes remained astonishingly constant (Table I) A likely explanation is that the essential changes which take place in connexion with pseudoexfoliation occur at an early stage Both the pathological increases in tension which result in glaucoma as well as the small increases in the tension level we have been able to trace in the remaining patients in our material may be assumed to arise during this early phase of the exfoliation process The exfoliation process would appear to be active within a limited period of time only after which it seems to calm down Thus what can be observed later on may therefore to some extent be regarded as a sequela of a process which has already taken place and which in the main has been concluded

Summary

In material comprising 63 men and 177 women with unilateral pseudoexfoliation and otherwise normal eyes a significantly higher level of tension was found in eyes with pseudoexfoliation compared with those in which this condition was not present The average difference in tension was 2.15 mm Hg in the men and 1.46 mm Hg in the women When comparing a group of patients 59 men and 88 women with bilateral pseudoexfoliation but otherwise normal eyes we found that the average difference in tension between the two eyes was much less There were significantly more patients with unilateral pseudoexfoliation in whom tension in the eye with pseudoexfoliation was clearly higher than in the other eye than there were patients in the group with bilateral pseudoexfo

liation in whom a clear difference in tension between the two eyes was observed

In a group of patients with unilateral pseudoexfoliation who had not developed glaucoma during the period of observation a record was kept of deviations in the ocular tension over a number of years. No tendency for the ocular tension to increase in eyes with pseudoexfoliation was observed. Our findings indicate that the essential changes which affect ocular tension take place during an early phase of the exfoliation process.

References

Aasved H Pseudoexfoliatio lentis ved masseundersøkelse i Bergen. Norwegian Ophthalm Soc. Stavanger 1964. To be published in *Acta Ophthalmol*

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THE IMPORTANCE OF THE POLYSACCHARIDES FOR THE NORMAL FUNCTION OF THE CORNEAL STROMA

BY

A. ANSETH and L. A. FRANSSON

A connective tissue consists of cells fibroblasts and a varying number of fibrillar elements collagen and elastin. The cells and fibrils are imbedded in an abundant ground substance where the polysaccharides or glycosaminoglycans are the most prominent components. The polysaccharides exert many functions. Because of their gel properties they prevent spreading of particles and substances in the tissue. Their water binding capacity is partly responsible for the fluid balance of the tissue. The polysaccharides are negatively charged and therefore link together the fibrillar elements in the tissue and to some extent determine the orientation of newly produced fibrils.

The corneal stroma is a specialized type of connective tissue. It contains relatively few cells keratocytes which are surrounded by tightly packed collagen fibrils. The fibrils generally have a small and uniform diameter and are oriented in lamellae parallel to the corneal surface. The polysaccharide content of corneal stroma is 4-5% of the dry weight. Approximately two thirds of the stromal polysaccharides consist of keratan sulfate. This polysaccharide is quite characteristic for the cornea as it is only found in relatively small amounts in a few other tissues in the body. The remaining one third is chondroitin-4-sulfate (Anseth & Laurent 1961, Laurent & Anseth 1961, Fransson & Anseth 1967). The regular structure of the corneal stroma is the anatomical basis for the transparency of the tissue its most important biological property. The transparency of the corneal stroma also depends on its water content. Nor

mally the tissue is in a state of relative dehydration depending on an active transport of water and ions across the endothelial cell layer. Thus a balance is maintained between this fluid transport and the osmotic pressure exerted by the macromolecules in the ground substance (Pirie & v Heyningen 1956).

Several inflammatory processes and injuries affecting the cornea diminish the endothelial "pump" activity resulting in a pathological swelling of the stroma which reduces the visual acuity. In less severe cases the edema may disappear completely and normal transparency may return. In more severe cases permanent damage to the endothelial cells may cause a chronic edema of the stroma in which non transparent scar tissue is eventually produced.

If a correlation exists between the polysaccharide pattern and the optical properties of the corneal stroma, changes in the composition of these substances would be expected during transient and permanent reduction of the stromal transparency. It is the purpose of this communication to present some experimental data which indicate that the above mentioned correlation really exists. Details concerning experimental data and materials and methods used are found in the original papers referred to in the text.

Experimental data

1 During the embryonic development in chicken an increase in corneal transparency has been demonstrated (Coulombre & Coulombre 1961). This is the result of a simultaneous decrease in the water content of the tissue. During the same period of time an increase in the polysaccharide content of the corneal stroma was found (Anseth 1961). The most striking increase occurred in a polysaccharide fraction containing highly sulfated keratan sulfate with a high molecular weight (eluted with 2.0 M Cl⁻) (Fig. 1). The rise in transparency and the increase in the above mentioned keratan sulfate fraction are closely related, indicating a correlation between keratan sulfate and corneal transparency.

2 The stromal edema which appears in connection with pathological conditions afflicting the cornea has been imitated experimentally in rabbits. A transient edema is produced by a careful removal of the endothelial cell layer; a permanent edema by removal of both the endothelium and the Descemet's membrane. In both cases a marked edema appears within a few hours of the operation. If only the endothelial cells are scraped off the edema slowly disappears after some weeks or months starting in the periphery of the cornea. When the inner surface of the cornea is covered by functioning cells the stroma is again transparent and free of edema. The loss of Descemet's membrane seems to prevent the cells from growing in and in these cases a permanent edema of the corneal stroma is created in which non transparent scar tissue appears.

POLYSACCHARIDES IN CHICKEN CORNEA DURING THE DEVELOPMENT

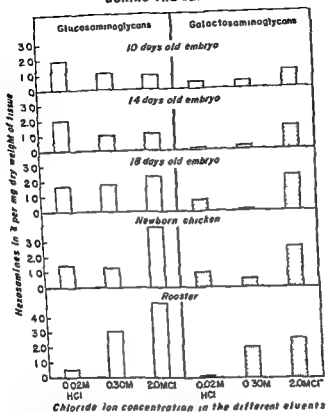


Fig 1

Distribution of polysaccharides from developing chicken corneas in ECTEOLA fractions (glucosaminoglycans = keratan sulfate galactosaminoglycans = chondroitin sulfate)

Analyses of the polysaccharide composition in these corneas at different times after surgery were performed (Anseth 1969a, Anseth & Fransson 1969). Fig. 2 shows the changes in the polysaccharide content during a transient stromal edema. Both the keratan sulfate and the chondroitin-4 sulfate content is reduced to approximately 50 per cent of their original values. This is a true loss of polysaccharides and not only a dilution effect because of the increasing water content of the tissue since the values are expressed as hexosamines per dry weight tissue. When the edema disappears the polysaccharide content increases again and 3 months after surgery when the edema has disappeared and the cornea has regained its transparency both polysaccharide fractions are normalized. No qualitative changes in the polysaccharides have taken place.

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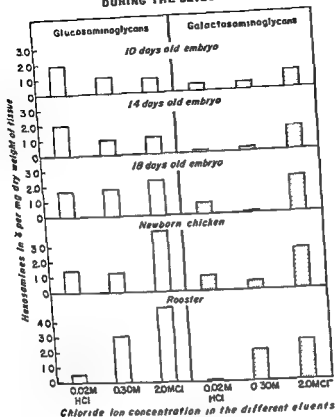


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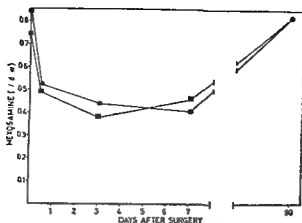


Fig 2

Polysaccharide content in various stages of transient stromal edema

Keratan sulfate ●—●
Chondroitin sulfate ■—■

during the period of edema since the elution pattern seems to be unchanged through the experiment (Fig 3)

The same loss of polysaccharides was found in edematous scar tissue produced by removal of endothelium and Descemet's membrane (Fig 4). In these corneas a chondroitin sulfate like polysaccharide was isolated and the analyses showed that it was dermatan sulfate, a polysaccharide normally *not* present in the cornea (Anseth & Fransson 1969). Fig 5 shows chromatograms of polysaccharides from normal cornea and from corneal scar tissue 4 and 7 weeks after surgery. A gradual accumulation of material eluted with an increasing ion strength is demonstrated in the scar tissue. This behavior is typical of dermatan sulfate.

Electron microscopy of corneal scars has shown that in this tissue normal corneal fibrils are replaced by coarse fibrils with a greater variety of diameter (Schwartz 1953, Jakus 1962). It is of interest to note that dermatan sulfate generally occurs in tissues containing coarse collagen fibrils of skin, tendons, sclera, vessel walls, etc. (Meyer, Davidson, Linker & Hoffman 1956). Although very little is known about the interactions between polysaccharides and collagen *in vivo*, it may be suggested that the presence of dermatan sulfate in the ground substance favors the formation of collagen fibrils with varying fiber diameter (Jackson & Bentley 1968).

The results referred to above indicate a correlation between corneal transparency and the polysaccharide pattern of the stroma. A transient loss of transparency caused by edema is correlated to quantitative changes in the polysaccharides. When a permanent loss of transparency caused by scar tissue for

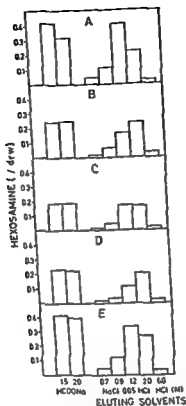


Fig 5

Analyses of normal cornea and edematous cornea at various stages by ECTEOLA formate microcolumn technique

A normal cornea B 12 hr edema C 3 day edema D 7 day edema E 90 days after surgery (healed)

The formate fractions corresponds to chondroitin 4 sulfate and a small amount of low sulfated keratan sulfate while the NaCl fractions contain keratan sulfate

mation develops a polysaccharide is produced which is normally not present in the cornea

It would be of interest to investigate if the changes in the polysaccharide pattern referred to above also takes place in human corneas suffering from different disorders For that reason corneal tissue obtained from the kerato plasty activity at the University Eye Clinic in Lund was divided in 4 different pools (*inseth* 1969b)

1 *keratoconus* without edema and scar formation

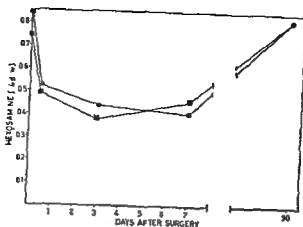


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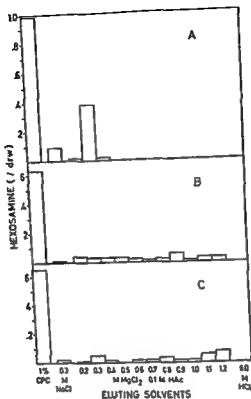


Fig 5

Analyses of normal cornea (A) and corneal scar tissue 4 weeks (B) and 7 weeks after surgery (C) using the CPC cellulose microcolumn technique

These results are in agreement with the data obtained in the experimental studies. A decrease in the polysaccharide content was found in those human corneas where a reduction in the transparency was due to corneal edema and scar tissue formation. Dermatan sulfate was demonstrated in corneal disorders where an active scar tissue formation could be expected namely in keratitis and lattice degeneration. In keratoconus the decrease in visual acuity is due to the pathological thinning of the cornea and its change of curvature and not to a reduction in the transparency of the tissue. In these corneas no quantitative or qualitative changes in the polysaccharide pattern could be demonstrated.

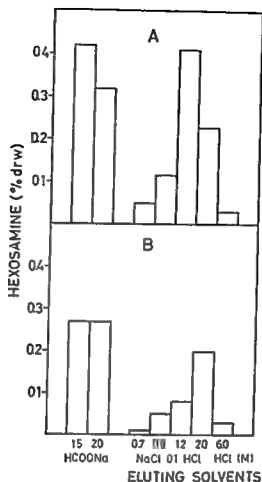


Fig 4

Analyses of normal cornea (A) and corneal scar tissue 6-7 weeks after surgery (B) by the ECTEOLA formate microcolumn technique

- 2 *keratitis* in an active phase with pathological edema and scar formation
- 3 *maculae corneae* representing a healed stage of keratitis without edema and
- 4 *lattice degeneration* in a relatively late stadium of the disease with pathological edema

Fig 5 shows chromatograms of polysaccharides from these four corneal disorders compared with normal human cornea. No pathological changes in the polysaccharide pattern was found in keratoconus whereas in the three others a decrease in the polysaccharide content especially in the keratan sulfate fractions could be demonstrated.

Dermatan sulfate was found in keratitis and lattice degeneration (Fig 7)

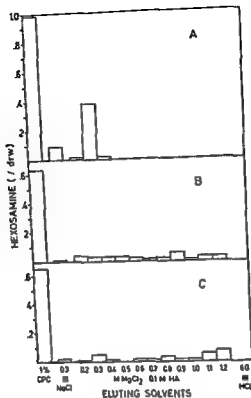


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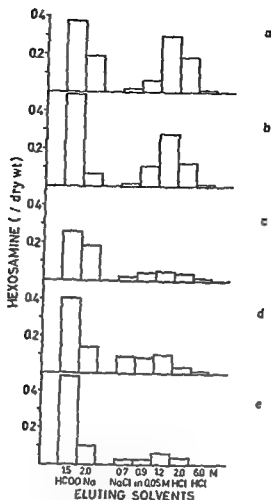


Fig 6

Analyses of normal and pathological human corneal tissue by the ECTEOLA formate microcolumn technique
a normal cornea b keratoconus c keratitis d maculae corneae e lattice degeneration

Summary

Experimental data indicating a correlation between the polysaccharide pattern and the optical properties of the corneal stroma are presented. During the embryonic development there is a close relationship between the rise in transparency and the increase in keratan sulfate of the corneal stroma. A transient loss of transparency caused by stromal edema is correlated to quantitative changes in the polysaccharides. When a permanent loss of transparency caused by scar tissue formation develops, dermatan sulfate is produced which is normally not present in the cornea.

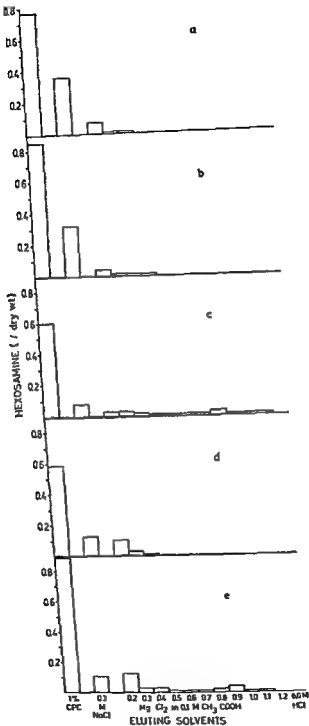


Fig 7

Analyses of normal and pathological human corneal tissue by the CFC-cellulose microcolumn technique

a normal cornea, b keratoconus c keratitis, d maculae corneae e lattice degeneration.

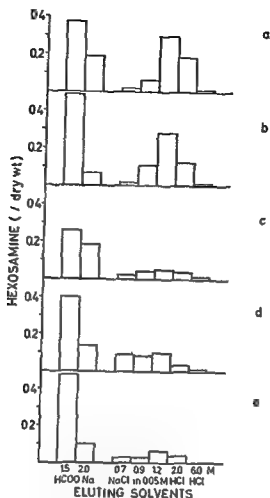


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Summary

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ANKYLOBLEPHARON FILIFORME CONGENITUM ASSOCIATED WITH HARELIP AND CLEFT-PALATE

BY

NIELS EHLERS and IB KRARUP JENSEN

Ankyloblepharon filiforme congenitum (or adnatum) indicates a malformation in which the margins of the upper and lower eyelids are connected by extensile tissue bands. In the literature 24 cases have been reported.

Lohlein (1930) showed a photograph of a baby with ankyloblepharon filiforme and an obvious cleft lip. Later this coincidence of malformations have been reported by Alianna (1957) and by Long & Blandford (1962). Van der Woude (1954) described a family with a strong occurrence of labial fistula, cleft lip and cleft palate in which one of the patients with labial fistula had unilateral ankyloblepharon filiforme. The present case brings the number of the coincidence of ankyloblepharon and harelip and/or cleft palate up to 5 out of a total of 24 cases of ankyloblepharon filiforme.

A total ankyloblepharon in most cases occurs associated with severe facial and ocular malformations. Berndorfer (1965) in a report of four cases with gross defects of the facial structures presented one with complete cleft lip and cleft palate associated with homolateral total ankyloblepharon and microphthalmos.

References

- Anseth A* (1961) *Exptl Eye Res* **1** 116
Anseth A (1969a) *Exptl Eye Res* **8** 297
Anseth A (1969b) *Exptl Eye Res* **8** 438
Anseth A & *Fransson L A* (1969) *Exptl Eye Res* **8** 302
Anseth A & *Laurent T C* (1961) *Exptl Eye Res* **1** 25
Coulombre A J & *Coulombre J L* (1958) *J Cell comp Physiol* **51** 1
Fransson L-A & *Anseth A* (1964) *Exptl Eye Res* **6** 107
Jackson D S & *Bentley J P* (1968) In *Treatise on Collagen* vol 2 part A p 181
 (Ed by Ramachandran G N and Gould B S) Academic Press London
Jakus M A (1962) *Invest Ophthalmol* **1** 202
Laurent T C & *Anseth A* (1961) *Exptl Eye Res* **1** 99
Meyer K, *Davidson E A*, *Linker A* & *Hoffman P* (1956) *Biochim Biophys Acta* **21** 506
Pirie A & *van Heyningen R* (1956) *Biochemistry of the Eye* p 144 Blackwell
 Scientific Publications Oxford
Schwart W (1953) *Zeitschr Zellforsch* **53** 78

The pathogenesis is not known so far. Inflammation of the lid margins causing defects in the epithelium (Hasner 1881, Mattson 1950) or traumatic lesions caused by fingernails scratching the epithelium (Wintersteiner 1908) have been proposed. However, no evidence of inflammation in any part of the eye or its adnexa has ever been presented in such cases (Khanna 1957). Probably an infection would also affect the development of the lashes and glands which have always been found normal. Explanation of the condition by trauma is difficult to accept since symmetrical bands in the two eyes may occur.

Khanna (1957) considers an anomaly in the separation process. To the present authors it seems much more probable in light of the coincidence of ankyloblepharon and harelip and cleft palate that the anomaly is caused by a maldevelopment related in time to the junction of the eyelids and palatine processes and working by mechanisms known from the normal development. A possible explanation might be defects in the subepithelial collagen fibres of the eyelids at the time of junction (30-40 mm c.r.l. 8-10 menstrual week).

Summary

A case of ankyloblepharon filiforme congenitum associated with harelip and cleft palate is reported. This coincidence of malformations has been observed in 5 out of 24 cases of ankyloblepharon filiforme. The possibility of common or related pathogenetic factors is considered.

References

- Andersen H, Ehlers V & Matthiessen M E (1965) *Acta ophthalmol* 43 642
 Andersen H, Ehlers V, Matthiessen M E & Claesson M H (1967) *Acta ophthalmol* 45 58
 Andersen H & Matthiessen M E (1968) *Acta anat* 68 413
 Berndorfer A (1963) *Arch f Kinderheilk* 119 160
 De Elder S (1964) *System of Ophthalmology* III p 869 London
 Hasner (1881) *Zschr f Augenheilk* 9 479
 Khanna V D (1957) *Amer J Ophthalmol* 43 774
 Lugg J C & Blandford S E (1962) *Amer J Ophthalmol* 53 176
 Lohlein W (1950) *Kurzes Handb d Ophthalmologie* III p 25 Berlin
 Mattson H (1950) *Acta ophthalmol* 3 723
 Van der Woude A (1954) *Amer J human Gen* 6 744
 Wintersteiner H (1908) *Arch f Augenheilk* 59 196

Case report

A newborn boy was admitted to the University Obstetric Clinic because of lactation difficulties due to complete cleft lip and cleft palate on the right side.

Examination of the eyes showed typical bilateral ankyloblepharon filiforme. On the right side the lid margins were connected by a single rather broad strand of tissue while on the left side several delicate strings occupied and partially closed the lateral half of the palpebral fissure. The lids showed no other malformations. The eyeballs were of normal size. Examinations of the anterior segments and ophthalmoscopy were normal.

The ankyloblepharon strands were severed surgically followed by healing without scar formation.

Pregnancy and delivery had been uncomplicated. The father and the father's sister both have harelip and cleft palate while the grandfather was known to have harelip only. No other cases of ankyloblepharon are known in the family. In the mother's family no malformations are known.

Comments

The incidence of harelip and cleft palate is 1.5 per thousand while ankyloblepharon filiforme is extremely seldom. The occurrence of harelip and cleft palate in 5 out of 24 cases of ankyloblepharon filiforme suggests common or related pathogenetic factors.

The eyelids develop as protruding folds above and below the eye visible already at the 12 mm stage (crown rump length 12 mm). At the 38-40 mm stage the upper and lower eyelids close in front of the eye. This junction is purely epithelial; mesodermal tissue does not break through the epithelium. Before the junction a very thick "basement membrane" is seen by light microscopy beneath the junctional epithelium. By electron microscopy the thick membrane is seen as a condensation of collagen and precollagen fibres close to the epithelial basement membrane (Andersen *et al.* 1965, 1967). Normally the eyelids reopen in the 6th to 7th foetal month.

Andersen & Matthiessen (1968) on a human foetal material studied the normal development of the face and made special reference to the development of harelip and cleft palate. Comparisons were made with the development of the eyelids. During the fusion of the palatine processes no subepithelial condensation of collagen was observed.

Microscopy of ankyloblepharon bands have been made several times (Duke Elder 1964) and have shown them to consist of a central vascular mesodermal tissue surrounded by squamous epithelium. Surgical sectioning of the bands, the simple and effective treatment, causes bleeding. The pathological process in ankyloblepharon filiforme is thus a penetration of the junctional epithelium by mesodermal tissue.

results of conventional methods – primarily the capsule forceps – with those of the cataract operations performed by means of cryoextractor

In general where cryosurgery has been used the results of cataract extractions have clearly been considered more successful (Jensen 1965 Rosengren & Enoksson 1966 Met 1967 Vitali 1967 Buschmann & Kartakchou 1968 Duguid 1968 Goldberg 1968 Vancea Niculescu & Hagopol 1968 Worthen & Brubaker 1968 Seedorff & Laxaet 1969) For example the number of intracapsular extractions in these materials varies between 82-100 per cent. The capsule rupture of a hypermature cataract also seems to occur easily in the cryoextractions but it is likely to occur even more easily when other methods are used. Certain authors have also noticed that results are slightly worse immediately after the employment of the procedure than in a later stage (e.g. Rosengren & Enoksson). According to many authors only the number of intracapsular operations increased with the cryosurgical technique (e.g. Worthen & Brubaker) although some have reported a reduced incidence of vitreous complications (e.g. Seedorff & Laxaet).

The disadvantages of the cryotechnique have naturally been investigated. The cryoextractor tip may adhere to the iris, cornea or sutures but this has not generally been considered the cause of permanent damage. Section should be slightly larger than in capsule forceps extractions – 180 degrees is generally enough to permit application and manipulation of the extractor tip. Maximum bending back of the cornea may be necessary; it is assumed that excessive manipulation of the cornea and inadvertent cooling/or freezing of the endothelial cells could produce persistent corneal damage (e.g. Taylor & Dalburg Jr 1963). According to several reports corneal complications have not increased and owing to the easier operative course of cryoextractions the operated eye is less apt to develop these reactions (e.g. Seedorff & Laxaet). Criticism has also been made about the overly large size of certain cryoextractors as well as that not all of them stay sufficiently cold for the required length of time.

Present study

Material and the operative technique

The material consists of 460 cataracts which were operated on using cryosurgery technique. The results of these operations are compared with the control group of 40 cataracts in which the lens has been extracted using capsule forceps and alphachymotrypsin. In the cryogroup the same enzyme was used in 300 cases (75 per cent). The number of the male and female cases according to different age and sex groups is presented in Table 1.

The cases were largely common senile and mature cataracts. The eyes with

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RESULTS OF CRYOEXTRACTIONS OF 460 CATARACTS COMPARED WITH 470 CAPSULE FORCEPS EXTRACTIONS

BY

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In 1961 one of the authors made a retrospective study in which results obtained from 470 cataract operations performed by using zonulolysis and an equal number of the same kind of operations without zonulolysis were compared to each other (Castrén 1961). It was verified then that there were noticeably better results with alphachymotrypsin. The following results reveal an especially significant statistical difference.

- 1) The ruptures of the lens capsules decreased in the enzyme group from 21 to 11 per cent.
- 2) Vitreous prolapses during the operation occurred in 13 per cent of the cases but in the group in which the enzyme was not used the corresponding percentage was 23 per cent.
- 3) After the cataract extraction 74 per cent of the enzyme group and 66 per cent of the control group had good vision (0.5-1.6).
- 4) Four per cent of the enzyme group and eight per cent of the control group had final vision less than 1 C 1 m or blindness.

In the same year that the study mentioned above was printed Arwawic published his cryoextraction method. Since then many results have been published about materials on which the procedure mentioned was used. But there are relatively few studies in which an attempt has been made to compare the

Table 2
Number of different cataracts

Type of cataract	Cryo group			Control group		
	Males	Females	Total	Males	Females	Total
Cataracta senilis hypermatura	8	8	16			
Cataracta senilis matura	135	181	314	76	174	250
Cataracta senilis ferematura	25	25	50	42	62	104
Cataracta complicata	30	26	56	16	37	53
Other cataracts	8	16	24	25	40	65
Total	204	256	460	157	313	470

technique When defrosting was required due to adherence of the tip to the iris cornea or section the other assistant has irrigated this place with warm saline After the delivery of the lens additional Barraquer's silk sutures were used - lately up to six-eight sutures due to the longer section Acetylcholin was injected into the anterior chamber or pilocarpin and eserine were instilled upon the eye The pupil was dilated on the second day - in some cases later after the operation steroid drops were instilled later The triangular silk suture was usually removed 8-12 days after the operation - Since 1966 cryoextraction of cataracts has been in routine use in our clinic The follow up time was from three months to four years

Results

Cryoextraction succeeded intracapsularly 421 times or in 91.5% of the cases (Table 3) The corresponding figures in the control group were 419 and 89.2%. The difference however was not statistically significant For those under 40 the capsule ruptured in three cases out of fourteen in the cryo group (21.4%) and in three out of eleven in the control group (27.3%)

In reference to complications occurring during the operation the cornea ad

Table 1
Number of cataract operations in different age and sex groups

Age in years	Cryo group			Control group		
	Males	Females	Total	Males	Females	Total
0-10	—	—	—	1	—	1
11-40	6	8	14	4	7	11
41-50	17	10	27	12	9	21
51-60	44	38	82	32	38	70
61-65	32	38	70	21	43	64
66-70	34	51	85	25	54	79
71-75	34	43	77	38	73	111
76-80	28	35	63	14	63	77
>80	9	33	42	■	26	35
Total	204	256	460	157	313	470

light perception vision were recorded as having mature cataracts. Hypermaturity was a diagnosis only where so stated in the operative notes or records. Table 2 shows the different forms of cataracts in the material.

Only a few of the operations were performed under general anaesthesia. After the usual pre medication (Pentobarbital 50-100 mg, Pethidin 50-100 mg, often Lergican 50 mg 1 hr before operation) and the facial nerve block (O'Brien and/or van Lint) retrobulbar injection was made. The bridge suture was passed by the insertion of the superior muscle. 1-0 triangular silk corneoscleral suture was inserted before opening the anterior chamber. Flieringa's ring was sutured in highly myopic eyes. A relatively short section was made up and then lengthened both nasally and temporally with scissors. After two peripheral iridotomies two appositional sutures, either Barraquer's silk or rat tail suture, were placed on both sides of the triangular suture. The enzyme was injected behind the iris, the anterior chamber and the section were irrigated with warm normal saline. In the control group the operator performed the delivery of the lens so that the corneal flap was raised by lifting the triangular suture with the left hand while applying the capsule forceps to the lens capsule with the right hand. The assistant pushed gently at 6 o'clock with the squint hook. In cryoextractions the operator removed the iris by using the pupil margin double retractor while applying the extractor at the same time on the upper part of the lens surface with his right hand. The assistant raised the corneal flap and dried the lens surface. In each case the delivery of the lens was attempted by the sliding

hered to the cryoextractor nine times (two per cent) and the iris 27 times (5.9%). Permanent injuries could not be shown in any of these cases

Cases of vitreous loss during the operation totalled 25 or 5.4 per cent in the cryo group but more than the double or 58 (12.6 per cent) in the control group (Table 4). The difference was highly significant

Vitreous prolapses after the operation occurred only twice in both the cryo and the control group (Table 5). Postoperative iris prolapses occurred in the former group 18 times (3.9 per cent) and in the control group only in nine cases (1.9 per cent). This difference however was not statistically significant

The cases of vitreous in the anterior chamber with ruptured anterior hyaloid membrane are presented in Table 6. Such cases occurred in the cryo group 39 times or in 8.5 per cent but in the control group 159 times or in 33.9 per cent. This difference was also highly significant

Table 4
Vitreous loss during the operation. Number of the cases

Sex	Control group		Cryo group	
	No loss of vitreous	Vitreous loss	No loss of vitreous	Vitreous loss
Males	191	11	137	20
Females	244	14	275	38
Total	435 (94.5%)	25 (5.5%)	412 (87.4%)	58 (12.6%)

Table 5
Number of cases with post operative vitreous and iris prolapses

Sex	Cryo group		Control group	
	Vitreous prolapse	Iris prolapse	Vitreous prolapse	Iris prolapse
Males	1	8	1	4
Females	1	10	1	5
Total	2 (0.4%)	18 (3.9%)	2 (0.4%)	9 (1.9%)

Table 3
Number of intra and extracapsular extractions

Sex	Cryo group			Control group		
	Intra	Extra	Total	Intra	Extra	Total
Males	170 (87.8%)	25 (12.2%)	204	132 (84.1%)	25 (15.9%)	157
Females	242 (94.5%)	14 (5.5%)	256	287 (91.7%)	26 (8.3%)	313
Total	421 (91.5%)	39 (8.5%)	460	419 (89.2%)	51 (10.8%)	470

(10.4 per cent) of the cryo group and in the control group in 70 cases (14.9 per cent). This difference was not statistically significant.

Post operative secondary glaucoma (Table 8) was detected in the cryo group in 17 eyes (3.7 per cent) and in the control group in 15 eyes (3.2 per cent). This difference was not significant.

Late retinal detachments occurred after the cataract operation (Table 8) in the cryo group in ten cases or in 2.2 per cent and in the control group in six cases (1.3 per cent). The difference was not statistically significant.

Vision after cataract operation in this material appears in Table 9. Information on visual acuity in four cases is unfortunately lacking. These patients either died or were moved after the operation to another hospital. Vision of 0.5-1.6 was obtained in 318 eyes (69.7 per cent) in the cryo group and in 340 eyes (74.0 per cent) in the control group. This difference was not statistically significant.

A very poor result - vision less than F.C. 1 m - was the final outcome in 23 cases (5.0 per cent) in the cryo group and in 19 cases (4.1 per cent) in the control group. The difference was not significant.

DISCUSSION

Since the quantities of the cryo and control material were the same (460-470 cases) and were operated on in the same way with the exception of the extraction itself, they are probably comparable. Since our clinic is a teaching hospital many different individuals have performed the operations (about 20 in both

Table 8

Number of cases of secondary glaucoma and retinal detachment after cataract surgery

Sex	Cryo group		Control group	
	Secondary glaucoma	Retinal detachment	Secondary glaucoma	Retinal detachment
Males	9	4	8	5
Females	8	6	7	1
Total	17 (3.7%)	10 (2.2%)	15 (3.2%)	6 (1.3%)

Table 6

Number of cases with post operative iritis uveitis and vitreous in the anterior chamber with ruptured ant hyaloid membrane

Sex	Cryo group		Control group	
	Iritis or uveitis	Vitreous in ant chamber	Iritis or uveitis	Vitreous in ant chamber
Males	18	15	12	54
Females	18	24	6	105
Total	36 (7.8 %)	39 (8.5 %)	18 (3.8 %)	159 (33.9 %)

Post operative iritis and uveitis (Table 6) occurred 36 times (7.8 per cent) in the cryo group but in only 18 cases (3.8 per cent) of the control group. This difference was significant. Iritis and uveitis cases lasting less than three weeks are not included in these figures since a slight irritation of iris is common after cataract operation.

Complications of the cornea (keratitis, descemetitis, oedema and vascularization of the cornea) lasting more than three weeks have been considered in Table 7. In the cryo group such complications occurred 19 times (4.1 per cent) and in the control group in 12 cases (2.6 per cent). However, this difference was not statistically significant.

Post operative choroidal detachments (Table 7) were ascertained in 48 cases

Table 7

Number of cases with post operative corneal complications and choroidal detachments

Sex	Cryo group		Control group	
	Corneal complications	Choroidal detachments	Corneal complications	Choroidal detachments
Males	7	23	6	28
Females	12	25	6	42
Total	19 (4.1 %)	48 (10.4 %)	12 (2.6 %)	70 (14.9 %)

materials) The first operations of about 16 doctors specializing in ophthalmology are included in the figures for both materials

One of the most common complications in cataract operations is the capsule rupture. It has decreased from 10.8 per cent of the control group to 8.5 per cent of the cryo group. This complication happened relatively more often with hypermature cataracts or when the cataracts of those under 40 years of age were being removed. However in operations on young patients for example capsule ruptures decreased from 21.3 per cent to 21.4 per cent.

Perhaps the most vexatious complication in cataract operations vitreous loss was brought down from 12.6% of the control material to 5.4% in the cryo group. This gratifying result was also highly significant statistically. In our opinion this might be due to the fact that it is not necessary to push the lens as much when performing the cryoextraction as when adhering to it with forceps; neither is so much counterpressure needed from outside of the eye. See dorff & Lavaetz also verify in the material from cases 2 & 413 that vitreous loss decreased in the cryo group to two per cent from the ten per cent of the forceps extraphake group.

We further verified that post operative hyaloid membrane rupture and vitreous in the anterior chamber occurred in only 8.5 per cent of our cryo extraction group in comparison with 33.9% in the control group. This was a highly significant difference.

In the cryo group we had post operative iritis lasting over three weeks in 7.8% of the cases but in only 3.8% in the control group. The difference was significant. It is difficult to determine the cause with certainty but the employment of the iris retractor may provide a clue in this respect. The instrument was in the operator's poorer hand and his attention was properly fixed on the lens and the tip of the extractor.

Keratitis descemetitis oedema and vascularization of the cornea appeared in 19 cases (41 per cent) in the cryo group and 12 cases (26 per cent) in the control group. The difference was not statistically significant. There were no cases in which adherence of the extractor to the cornea could be cited as a cause of complications. Otherwise such adhering occurred in only two per cent of the operations.

In the interest of the severe complications of the cornea, six cases operated on during the earlier period of the cryosurgery of cataracts should be presented. The preoperative diagnoses were the following:

Chronic uveitis with secondary glaucoma in one case; three cases were complicated by glaucoma with accompanying endothelial degeneration. The cataract extraction was performed also in an eye having perforating injury and a probable phakic anaphylactic uveitis. In two cases the cornea seemed to be normal before the operation. - The age of the patients was between 58-82 years excepting one of 43 years (with corneal perforation).

Table 9
Final vision after cataract operations

Vision	Cryo group			Control group		
	Males	Females	Total	Males	Females	Total
0-FC 1 m	7	16	23 (50 %)	8	11	19 (41 %)
1 C 1 m-FC 5 m	7	15	22	11	14	25
0 1-0 4	28	65	93	20	57	77
0 5-1 6	158	160	318 (69 7 %)	117	228	345 (74 0 %)
Total	200	256	456	156	310	466

materials) The first operations of about 16 doctors specializing in ophthalmology are included in the figures for both materials

One of the most common complications in cataract operations is the capsule rupture. It has decreased from 10.8 per cent of the control group to 8.5 per cent of the cryo group. This complication happened relatively more often with hypermature cataracts or when the cataracts of those under 40 years of age were being removed. However, in operations on young patients for example capsule ruptures decreased from 27.3 per cent to 21.4 per cent.

Perhaps the most vexatious complication in cataract operations, vitreous loss, was brought down from 12.6% of the control material to 5.4% in the cryo group. This gratifying result was also highly significant statistically. In our opinion this might be due to the fact that it is not necessary to push the lens as much when performing the cryoextraction as when adhering to it with forceps; neither is so much counterpressure needed from outside of the eye. See Dorff & Lavaetz also verify in the material from cases 2 X 413 that vitreous loss decreased in the cryo group to two per cent from the ten per cent of the forceps extracapsular group.

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In the cryo group we had post operative iritis lasting over three weeks in 1.8% of the cases but in only 3.8% in the control group. The difference was significant. It is difficult to determine the cause with certainty, but the employment of the iris retractor may provide a clue in this respect. The instrument was in the operator's poorer hand and his attention was properly fixed on the lens and the tip of the extractor.

Keratitis, descemetitis, oedema and vascularization of the cornea appeared in 13 cases (4.1 per cent) in the cryo group and 12 cases (2.6 per cent) in the control group. The difference was not statistically significant. There were no cases in which adherence of the extractor to the cornea could be cited as a cause of complications. Otherwise such adhering occurred in only two per cent of the operations.

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In all cases the extraction succeeded intracapsularly *alphachymotrypsin* was used but additional silk — up to six apposition sutures in one case — were needed — In all cases the postoperative course was complicated by a severe uveitis Damage of the endothelium and persistent opacification of the cornea occurred in five patients Epithelial cell growth into the anterior chamber was suspected but ingrowth could be verified histologically after enucleation only in that case with scarred corneal wound due to injury

On the basis of these clinical observations some correlations seem obvious

-- The relatively large size of the cryoextractor used in these operations the reduced temperature gradient chemical irritation and the larger section combined with excessive manipulation of the cornea might be influenced hazardously on the metabolism of the cornea of these patients who already had a reduced endothelial function — Additional silk sutures due to a longer section may play a significant role in cases of suspected epithelial elements in the anterior chamber though this could not be confirmed

In general we felt the small number of corneoscleral sutures we have mostly used was the preventive factor explaining the small incidence of epithelial downgrowth in our clinic (Vannas 1957) Furthermore our most important suture the preplaced triangle suture of Vannas passed over the wound excluding any suture tracts to lead into the anterior chamber

In relation to choroidal detachments post operative glaucoma late retinal detachments and the final visual acuity of those operated on statistical differences did not appear

In conclusion it can be said on the basis of this study that cryoextraction seems to be the safest procedure for cataract operation at the present It is suited for difficult cases but according to our experience on some occasions the risks should be carefully compared with the benefits of this method

Summary

The material consisted of 930 cases of cataract extraction in the University Eye Clinic in Helsinki 460 were operated on using cryoextraction (lately extractor model Stahl) and 470 extractions (the control group) were made using *alpha* chymotrypsin and capsule forceps In the cryoextraction group zonulolysis was used in 77 per cent of the cases All 930 operations were tried to do by means of the intracapsular method

The operation succeeded intracapsularly in 91.5 per cent of the cryogroup and in 89.2 per cent in the control group The difference was not statistically significant

The cornea adhered to the cryoextractor nine times (two per cent) and the

itis 24 times (59 per cent) Permanent damage from these complications could not be observed

Vitreous loss during the operation occurred more rarely (5.4 per cent) in the cryo group than in the control group (12.6 per cent) This difference was highly significant

Post operative vitreous prolapses occurred in both groups only twice Post operative iris prolapses occurred in 39 per cent of the cases in the cryo group and in 19 per cent of the control group This difference was not significant

Vitreous in the anterior chamber with ruptured anterior hyaloid membrane occurred only in 8.5 per cent of the cryo material but in 33.9 per cent in the control group The difference was highly significant

Iritis or uveitis lasting more than three weeks after the operation was detected in 7.8 per cent in the cryo group but only in 3.8 per cent in the control group The iris retractor was suspected to be one of the causes of this complication

In relation to corneal complications as well as choroidal detachments secondary glaucoma retinal detachments and the final visual acuity statistical differences were not verified

On the basis of this study cryoextraction is considered the safest procedure for cataract operations for the present The possible causes of corneal complications are considered in details in the discussion

References

- Bichmann W & A Karkakelou Zur Kryoextraktion der Linse Klin Mbl Augenbk 195 1549
- Castro J A To use or not to use zonulolysis in cataract surgery? A study of the results of 340 operations Acta Ophth 1961 39 609
- Daglid M Cryo extraction of the Lens Trans Ophthal Soc U K 1963 38 125
- Eldberg H A Cataract Surgery by Cryo extraction. Int Surg 1963 50 109
- Jensen V A Cryoextraction with liquid nitrogen Acta Ophth 1965 43 803
- Kraus T Intracapsular Extraction of Intumescent Cataract by Application of Low Temperature Brit J Ophth 1961 45 9
- Mel H S Cryoextraction of Lens NY St J Med 1967 67 3247
- Peterson B & P Ekesson Cryoextraction - Results in 315 cases Acta Ophth 1966 44 431
- Seliff H H & B Lawaet Intracapsular Cataract Extraction by the Cryotechnique and Other Methods. A Comparative Study of 86 Cases. Acta Ophth 1969 4 61
- Taylor D M & Lewis J Dalburg Corneal Complications From Cryoextraction of Cataracts Arch Ophth 1969 93
- Vinca P, Mar a Nicolaeu & Viktoria Hagopoul Nos Experiences En Cryochirurgie Du Cristallin Ann Ocul 1969 91 63

In all cases the extraction succeeded intracapsularly, alphachymotrypsin was used but additional silk — up to six apposition sutures in one case — were needed — In all cases the postoperative course was complicated by a severe uveitis. Damage of the endothelium and persistent opacification of the cornea occurred in five patients. Epithelial cell growth into the anterior chamber was suspected but ingrowth could be verified histologically after enucleation only in that case with scarred corneal wound due to injury.

On the basis of these clinical observations some correlations seem obvious.

— The relatively large size of the cryoextractor used in these operations, the reduced temperature gradient, chemical irritation and the larger section combined with excessive manipulation of the cornea might be influenced hazardously on the metabolism of the cornea of these patients who already had a reduced endothelial function. — Additional silk sutures due to a longer section may play a significant role in cases of suspected epithelial elements in the anterior chamber though this could not be confirmed.

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In relation to choroidal detachments, postoperative glaucoma, late retinal detachments and the final visual acuity of those operated on, statistical differences did not appear.

In conclusion it can be said on the basis of this study that cryoextraction seems to be the safest procedure for cataract operation at the present. It is suited for difficult cases but according to our experience on some occasions the risks should be carefully compared with the benefits of this method.

Summary

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References

- Buschmann W & A Karakchou Zur Kryoextraktion der Linse Klin. Mbl. Augenhk. 1968 153 428
- Castren J A To use or not to use zonulolysis in cataract surgery? A study of the results of 940 operations Acta Ophth. 1961 39 608
- Duguid I M Cryo extraction of the Lens Trans. Ophthal. Soc. U.K. 1968 88 125
- G. Idberg H A Cataract Surgery by Cryo extraction Int. Surg. 1963 30 109
- Jensen V A Cryoextraction with liquid nitrogen Acta Ophth. 1965 43 803
- Krawiec T Intracapsular Extraction of Intumescent Cataract by Application of Low Temperature Brit. J. Ophth. 1961 45 29
- Met H S Cryoextraction of Lens N.Y. St. J. Med. 1967 67 3247
- Rosengren B & P Enoksson Cryoextraction - Results in 375 cases Acta Ophth. 1966 44 431
- Schorff H H & B. Lauact Intracapsular Cataract Extraction by the Cryotechnique and Other Methods A Comparative Study of 826 Cases Acta Ophth. 1969 47 761
- Taylor D M & Lewis A Dalburg Corneal Complications From Cryoextraction of Cataracts Arch. Ophth. 1968 9 3
- Vaneca P Maria Niculescu & Viktoria Hagiopol Noş. Experiences En Cryochirurgie Du Cristallin Ann. Oculist. 1968 901 832

- Vannas M* The intracapsular cataract operation -- Experiences and suggestions *Ophthalmologica* 1949 118 866
- Vannas S* Epithelial Downgrowth into the anterior chamber and deep into the eye
A case report *Acta Ophth* 1957 35 190
- Vitali G* La crioestrazione della cataratta *Studi Sassaresi* 1961 45 69
- Worthen David M & Richard F Brubaker* An Evolution of Cataract Cryoextraction
Arch Ophth 1968 79 8

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EXPERIMENTAL OBSERVATIONS ON THE REFLECTION AND INTERFERENCE PHENOMENON OF THE ULTRASOUND CAUSED BY ORBITAL FAT AND MUSCULAR TISSUES

BY

ARVO OKSALA and ANJA NIIRANEN

In its refraction and reflection ultrasound follows the same laws as light. Under certain circumstances refraction is followed by total reflection. When ultrasound passes from one substance into another that has a higher sound velocity the angle of refraction is greater than the angle of incidence. When the angle of refraction becomes greater than 90° the result is total reflection. The relation between the angles of incidence and refraction depends on the velocity of sound in the particular substances.

The refraction and reflection of ultrasound in the eye and orbit have been examined very little. Oksala & Hakkinen (1969) have found out that if the ultrasound hits the cornea and sclera at a 70° angle of incidence a total reflection is often observed. When the ultrasound meets the surface of the lens at the same angle (10°) the result may also be a total reflection (Oksala 1969).

In this experimental study we have tried to find out if the fat and muscular tissues of the orbit can reflect ultrasound and how high is the sound pressure in a reflected sound beam. At the experiments we observed under certain circumstances a strong increase in sound pressure as compared with control tests and this has been thought to be due to an interference phenomenon or to a focusing effect of the tissues.

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- Vannas M* The intracapsular cataract operation – Experiences and suggestions *Ophthalmologica* 1949 118 866
- Vannas S* Epithelial Downgrowth into the anterior chamber and deep into the eye. A case report *Acta Ophth* 1957 35 190
- Vitali G* La crioestrazione della cataratta *Studi Sassaresi* 1967 45 69
- Worthen David M & Richard F Brubaker* An Evolution of Cataract Cryoextraction *Arch Ophth* 1968 79 8

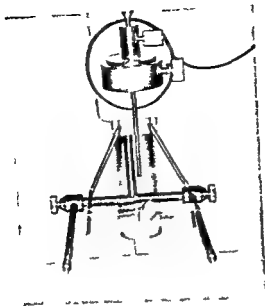


Fig 2

Above one can see a barlike transducer of 7.5 Mc/2 mm and beneath this between the copper wires there is a piece of orbital muscle and further down the steel ball

passed the center of the transducer. The intensity of the equipment was kept all the time at the same level (db reserve = 10) which is a level that is often used also in clinical diagnosis.

When the transducer is moved, one obtains various echo amplitudes which are directly proportionate to the sound pressures at the corresponding points. Control curves were obtained when the examination was carried out in water without any tissues.

Reflection was studied with 12 different pieces of muscular and fat tissue. At these examinations the angle of incidence in relation to the tissue was approximately 10° .

The interference and strengthening phenomenon was clearly observable in echo amplitude curves when the angle of incidence was about 10° . For these examinations also 12 different pieces of muscular and fat tissue were used.

Results

When the angle of incidence was about 10° , one could always, whenever it was wanted, produce a total reflection with both muscular and fat tissue. As the

The ultrasonic equipment was Kretztechnik's model 7000. The frequency of the transducer was 7.5 Mc and its diameter 2 mm. For the measurement of the sound fields we had constructed an instrument shown in Fig. 1. There the transducer is fixed to a stand and beneath the transducer we have a vessel full of water in which a SKF steel ball (diameter 1.5 mm) is moved. The position of the steel ball in relation to the transducer can be measured from three directions with a 0.1 mm accuracy. Fat and muscular tissues were prepared from the orbits of recently killed pigs. The muscular tissue was taken from the outer muscles of the eye. Plates of fat tissue were found from the vicinity of eye muscles. The thickness of muscular tissue was 4.6 mm and that of fat tissue 2.4 mm.

The examination took place in the far field of the transducer, the distance of the ball from the transducer being 30 mm. Pieces of fat or muscular tissue were fixed between copper wires so that the distance from the transducer to the anterior surface of the tissue was about 15 mm (Fig. 2). The copper wires were outside the sound field. During the examinations the ball was moved so that it

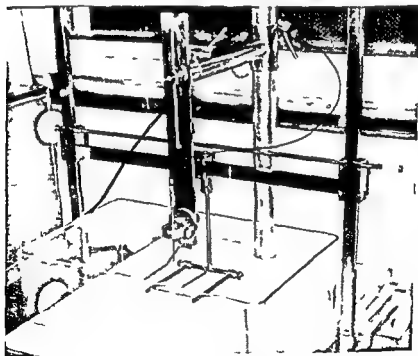


Fig. 1

The figure represents an apparatus that has been built for the measurements of sound fields. The transducer is fixed to a stand and beneath it there is a vessel filled with water in which a steel ball of 1.5 mm can be moved in three different directions.

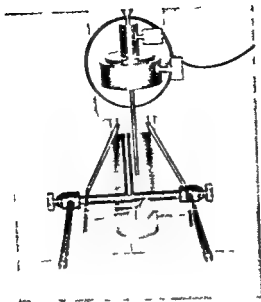


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Reflection was studied with 12 different pieces of muscular and fat tissue. At these examinations the angle of incidence in relation to the tissue was approximately 10° .

The interference and strengthening phenomenon was clearly observable in echo amplitude curves when the angle of incidence was about 60° . For these examinations also 12 different pieces of muscular and fat tissue were used.

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Equipment, material and research methods

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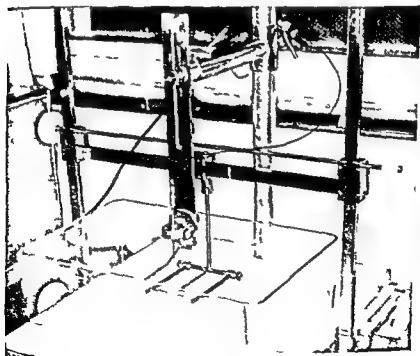


Fig. 1

The figure represents an apparatus that has been built for the measurements of sound fields. The transducer is fixed to a stand and beneath it there is a vessel filled with water in which a steel ball of 1.5 mm can be moved in three different directions.

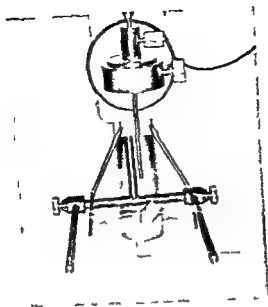


Fig 2

Above one can see a barlike transducer of 7.5 Mc/2 mm and beneath this between the copper wires there is a piece of orbital muscle and further down the steel ball

passed the center of the transducer. The intensity of the equipment was kept all the time at the same level (db reserve = 10) which is a level that is often used also in clinical diagnosis.

When the transducer is moved one obtains various echo amplitudes which are directly proportionate to the sound pressures at the corresponding points. Control curves were obtained when the examination was carried out in water without any tissues.

Reflection was studied with 12 different pieces of muscular and fat tissue. At these examinations the angle of incidence in relation to the tissue was approximately 10° .

The interference and strengthening phenomenon was clearly observable in echo amplitude curves when the angle of incidence was about 60° . For these examinations also 12 different pieces of muscular and fat tissue were used.

Results

When the angle of incidence was about 10° one could always, whenever it was wanted, produce a total reflection with both muscular and fat tissue. As the

examination with the steel ball covers only one cross section of the sound field at a time sometimes the search for the total reflection took a little longer sometimes a little less Finding the total reflection was easier with muscular than with fat tissue Fig 3 shows typical examples of total reflection in muscular and fat tissue The readings of the abscissa denote millimeters and those of the ordinate relative echo amplitudes The curve on the right represents a typical regular echo amplitude curve obtained in water The two echo amplitude curves on the left which consist of a continuous line have originated from a total reflection caused by a muscle while the curves that are made of a discontinuous line have been produced by a total reflection by fat tissue Muscular and fat tissues have reflected the sound beam and at those points of the sound field where measurements have been made one can observe fairly high sound pressures as compared with those of the control curve

Fig 4 represents typical examples of the changes in the sound field caused by muscular and fat tissues when the angle of incidence is approximately 60° On the right we have again a typical control curve obtained in water The curves on the left that are made of a continuous line have been obtained from muscular tissue and the ones with a discontinuous line from fat tissue All measurements gave similar echo amplitude curves We can see that muscular and fat tissues bring forth strong maxima and minima in the echo amplitude curves The maxima may considerably surpass the maximum of the control curve After passing through muscular or fat tissue the sound fields are definitely narrower

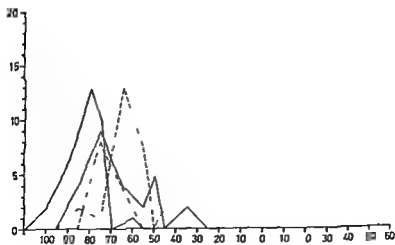


Fig 3

The figure shows the total reflection of ultrasound caused by muscular and fat tissue On the right we have the control curve obtained in water and on the left the echo amplitude curves obtained with muscular tissue (continuous line) and fat tissue (discontinuous line)

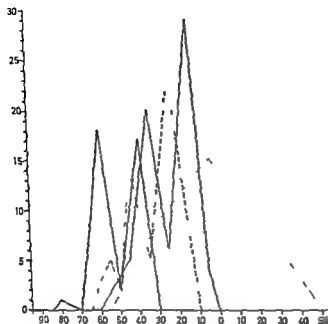


Fig 4

The figure represents the curves that were obtained when the ultrasound passed through muscular tissue (continuous line) and fat tissue (discontinuous line) at an angle of approximately 60°. The maxima may considerably surpass the maximum of the control curve on the right.

than in the control curve and in relation to the control curve they seem to have become somewhat dislodged

Comments

The results show that at a particular angle of incidence orbital muscular and fat tissues may cause a total reflection in ultrasound. In spite of the fact that we were not able to examine more than one cross section of the sound field with the steel ball, relatively high echoes were registered. It is possible that if several cross sections had been examined even higher echoes could have been found because the sound beam could also become dislodged at the same time that it was reflected.

It is by no means new to the authors of this paper that after ultrasound has travelled through some tissue a few millimeters thick one can still measure

examination with the steel ball covers only one cross section of the sound field at a time sometimes the search for the total reflection took a little longer, sometimes a little less Finding the total reflection was easier with muscular than with fat tissue Fig 3 shows typical examples of total reflection in muscular and fat tissue The readings of the abscissa denote millimeters and those of the ordinate relative echo amplitudes The curve on the right represents a typical regular echo amplitude curve obtained in water The two echo amplitude curves on the left which consist of a continuous line have originated from a total reflection caused by a muscle while the curves that are made of a discontinuous line have been produced by a total reflection by fat tissue Muscular and fat tissues have reflected the sound beam and at those points of the sound field where measurements have been made one can observe fairly high sound pressures as compared with those of the control curve

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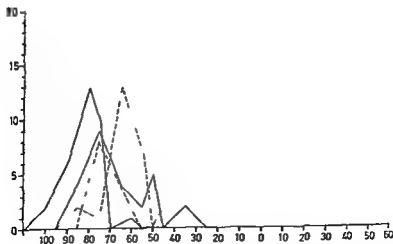


Fig 3

The figure shows the total reflection of ultrasound caused by muscular and fat tissue On the right we have the control curve obtained in water and on the left the echo amplitude curves obtained with muscular tissue (continuous line) and fat tissue (discontinuous line)

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EXPERIMENTAL STUDIES ON THE ECHOGRAM OF THE HUMAN LENS

BY

ARVO OKSALA and ANJA NIIRANEN

The extensive literature on the ultrasonic diagnosis of eye diseases contains only a few works that deal with the acoustic structure of clear and opaque human lenses and the relations between the optic and acoustic structures.

According to previous observations an optically clear or almost clear lens is also acoustically homogeneous i.e. its interior part will not reflect any echoes. But if there is a distinct nucleus in a cataract human lens its both surfaces will reflect an echo (Oksala & Lehtinen 1960). When 3 clear and 26 opaque lenses were examined with a transducer of 18 Mc/5 mm it was discovered that all clear lenses were acoustically homogeneous although the opaque lenses also included 6 acoustically homogeneous specimens (Oksala 1961). These results led to the conclusion that the interior part of an opaque lens reflects echoes just in case it contains a clearcut solid nucleus. When 15 clear and 15 opaque lenses were examined both clinically and experimentally with a 12 Mc/4 mm transducer all optically transparent lenses were found to be acoustically homogeneous and all cataract lenses acoustically unhomogeneous. This led to the fact that on the basis of echograms alone it was possible to determine if the lens would be optically distinctly opaque (Oksala & Varonen 1965).

Baum (1965) has also verified the acoustic unhomogeneity of the cataract lens and has drawn attention to the diagnostic significance of this phenomenon. McI & Bronson (1969) examined clinically an unselected series of fifty pre-

sound fields with clear minima and maxima in the far field. The appearance of strong maxima may be due to various reflections of ultrasound inside the tissue or to focusing effect of the tissue. The changes in the position of the sound fields in relation to the control field may be caused by reflection and refraction that take place inside the tissue.

The clinical significance for orbital examinations of the changes in the sound field that have now been discovered cannot be estimated on the basis of this investigation. When looked at theoretically, refraction, reflection and strengthening phenomenon may lead to localization errors in A scan and to a distorted picture in B scan.

Summary

At an experimental investigation it was found out that when the angle of incidence is approximately 70° the orbital muscular and fat tissues may cause a total reflection in ultrasound. After the ultrasound had passed through muscular or fat tissue one could even in the far field measure echo amplitude curves with high maxima and low minima. The maxima may be due to various reflections inside the tissue or to focusing effect of the tissues. Total reflection and interference may have clinical significance especially at the ultrasonic examinations of the orbit.

References

- Oksala A. Unpublished observation 1969
Oksala A & Hakkinen L. Experimental studies of the behavior of ultrasound in the sclera and cornea. In *Ophthalmic ultrasound* ed by Gitter, Keeney, Sarin and Meyer. Pp 59-64. Mosby, Saint Louis 1969.

+ 4 C The axial diameter of 43 lenses was measured with a sliding scale The diameter varied between 5.4 and 6.4 mm The axial diameters of the clear lenses were 6.0, 6.2 and 6.4 mm

Results

1 The echogram of a clear lens

Fig 1 shows the echogram of the optically clear lens of a 43 year old patient In all axial examinations the lens proved out to be acoustically homogeneous also when the db reserve = 3 Similarly the optically clear lens of a 50 year-old person was acoustically homogeneous

The third lens came from a 63 year old person whose visus was 1.3 but at a slit lamp examination the center of the lens appeared to be somewhat yellowish Optically the nuclei were a little more clearly outlined than normally Fig 2 shows the echogram of this lens It proves the lens acoustically heterogeneous The change in acoustic impedance at both surfaces of the nucleus is probably so distinct that separate echoes are reflected from them

2 Cataracta ferematura

There were 7 lenses altogether and the respective visus before the operations were 3×0.08 and 4×0.06 One of the lenses reflected three echoes viz two echoes from the anterior part and one from its posterior surface The echograms of other lenses had 4-5 echoes One of these with 5 echoes is seen in Fig 3 The central parts of the nuclei in these lenses were acoustically homogeneous



Fig 1

The echogram from the optically clear lens of a 43 year old patient The initial impulse on the left is followed by the echoes from both surfaces of the lens The lens proper is acoustically homogeneous

operative patients with senile cataracts. In conclusion of the paper they say that senile cataracts cause abnormal ultrasound patterns: the amount of opacity found in the anterior cortex and nucleus by slit lamp correlates semiquantitatively with the ultrasound appearance and the sum of opacities throughout the lens as seen clinically can be predicted by ultrasound with a validity adequate for clinical work.

The purpose of the study

On the basis of the earlier results mentioned above we have investigated the echograms of clear and cataract lenses and have made an attempt to clarify the relations between the optic and acoustic structure with reference to various opacities in the lens. In addition to that we have studied the attenuation of ultrasound in clear and opaque lenses in comparison with that in water.

Research equipment, material and method

For our investigation we used Kretztechnik's model 7000 and a 7.5 Mc/2 mm transducer. The amplification of the equipment was relatively high: i.e. the db reserve was either 5 or 15.

The material comprised 3 clear, 7 cataracta ferematura and 36 cataracta matura lenses. Clear lenses were obtained from eyes that had been removed because of choroidal melanomas.

The transducer was fixed to a stand and beneath it we placed a loop that had been made of copper wire. The lenses were then put onto the loop so that the loop itself was outside the sound field. The distance of the transducer from the anterior surface of the lens was 5 mm. The sound beam was always directed as axially as possible through the lens. The examination was carried out in a vessel filled with water. One or more photos were taken from an echogram of each lens.

The test object that we used to examine the attenuating effect of the lens was a steel ball with a diameter of 1.5 mm. This ball was moved so that it passed the center of the transducer at a distance of 25 mm. The amplitudes of the highest echoes were compared with one another by the amplification control device of the equipment which is fitted with a db scale. In these measurements we used 3 clear and 17 cataracta matura lenses.

During the interval between the enucleation and the examination (6-24 hours) the lenses were kept in Ringer solution in a refrigerator at a temperature of

+ 4°C The axial diameter of 43 lenses was measured with a sliding scale. The diameter varied between 5.4 and 6.8 mm. The axial diameters of the clear lenses were 6.0, 6.2 and 6.4 mm.

Results

1. The echogram of a clear lens

Fig. 1 shows the echogram of the optically clear lens of a 43 year old patient. In all axial examinations the lens proved out to be acoustically homogeneous also when the db reserve = 5. Similarly the optically clear lens of a 50 year old person was acoustically homogeneous.

The third lens came from a 63 year old person whose visus was 1/3 but at a slit lamp examination the center of the lens appeared to be somewhat yellowish. Optically the nuclei were a little more clearly outlined than normally. Fig. 2 shows the echogram of this lens. It proves the lens acoustically heterogeneous. The change in acoustic impedance at both surfaces of the nucleus is probably so distinct that separate echoes are reflected from them.

2. Cataracta ferematura

There were 7 lenses altogether and the respective visus before the operations were 3×0.03 and 4×0.06 . One of the lenses reflected three echoes viz. two echoes from the anterior part and one from its posterior surface. The echograms of other lenses had 4 or 5 echoes. One of these with 5 echoes is seen in Fig. 3. The central parts of the nuclei in these lenses were acoustically homogeneous.



Fig. 1

The echogram from the optically clear lens of a 43 year old patient. The initial im pulse on the left is followed by the echoes from both surfaces of the lens. The lens proper is acoustically homogeneous.



Fig 2

The echogram of the optically almost clear lens of a 68 year old patient with the initial impulse on the left. The echoes come from the surfaces of the lens and its nucleus.

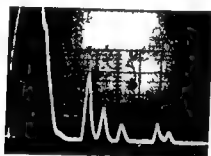


Fig 3

The echogram of a cataracta ferematura lens where the lens reflects 5 echoes. The center of the lens is acoustically homogeneous.

■ Cataracta matura

Of the 36 lenses one was of the cataracta nigra type. All lenses that were examined proved out to be acoustically clearly heterogeneous. Among the 10 photos that were taken from the echograms 4 different types could be distinguished. These are represented in Fig 4. The echogram in Fig 4 A shows two or three high echo peaks that are reflected from the anterior part of the lens. The central part of the lens is acoustically homogeneous and the posterior surface of the lens reflects one or two low echoes. In the form that is shown in Fig 4 B and obtained e.g. from the cataracta nigra case the echogram has clear echoes from both surfaces of the lens and the nucleus while the content of the nucleus seems to be acoustically rather homogeneous. In Fig 4 C the lens reflects several compact, fairly high and narrow echoes. When the position of the transducer was changed the amplitudes and positions of the highest echoes

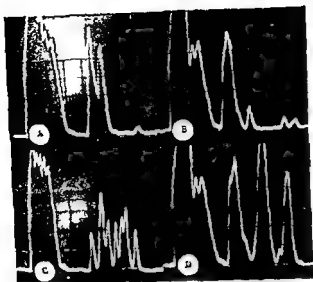


Fig 4

Four different types of echograms that were obtained from cataracta matura lenses. In A the anterior part of the lens reflects 2-3 high echoes and its posterior part 1-2 low echoes. In B the surfaces of the lens and its nucleus reflect an echo each while the center of the lens is acoustically homogeneous. In C the lens reflects several compact echoes and in D there are some less densely situated echoes.

showed some variation. The lens in Fig 4 D reflects 3 or 4 high and less densely situated echoes.

When the attenuation of ultrasound caused by the lens was measured, it was discovered that compared with water the amplitude of the highest echo in sound field was attenuated by 12-32 db by the lens. In 14 cases out of 19 the decrease in the echo was 21-25 db. There was no observable difference in the attenuation of ultrasound between the clear and opaque lenses.

Discussion

According to earlier observations an optically clear lens has also been acoustically homogeneous. In this investigation however the lens that had been removed from the 63 year old patient with the visus of 1/3 appeared to be acoustically somewhat heterogeneous as both surfaces of the nucleus reflected an echo even if no clear pathological opacity was optically observable. Among 7 cata-

racta feremature lenses one was acoustically homogeneous apart from the anterior part of the lens

On the basis of clinical ultrasonic investigations we know that the optically clear lens is almost always also acoustically homogeneous. As the optic and acoustic examinations and registrations differ a great deal from each other by their very nature it is to be expected that the optic and acoustic examinations of clear or a little opaque lenses at least in older people may yield the kind of controversial results that were obtained from the lens of 63 year old patient. The nucleus of the lens may acoustically come out more clearly than at an optic examination and vice versa.

All 36 cataracta matura lenses proved out to be both optically and acoustically distinctly heterogeneous. On the basis of their form the echograms of opaque lenses could be divided into 4 groups. In the first two groups the center of the nucleus in the lens was acoustically rather homogeneous as was the case also in cataracta ferematura lenses. In the third and fourth group the entire lenses were highly heterogeneous.

This work shows that on the basis of echograms alone one can often draw rough conclusions of the optic transparency of lenses. If a lens is acoustically completely homogeneous it will also be optically clear. If the echogram contains only the echoes of the lens and both surfaces of its nucleus the optic transparency of the lens in older people cannot be predicted on the basis of the echograms. If the entire area of the lens reflects echoes we have a case of a cataracta matura lens. An acoustic examination of the lens may be very useful in cases where an optic examination is impossible due to some opacities of the cornea or a seclusion or occlusion of the pupils.

Measurements of the thickness of the lenses indicated that during the storage the lenses had swelled about 2 mm. This fact did not affect the echograms of the two optically clear lenses but it is possible that it may have had an effect on the acoustic structure of the clear lens of the 63 year old patient making it a little more heterogeneous. It is improbable that this swelling should have changed the decisive factors in the acoustic structure of the cataracta ferematura and matura lenses, i.e. the surfaces of the lenses and their nuclei. The experimental results obtained from cataracta matura lenses correspond to previous clinical observations.

Summary

The material of this study consisted of 46 human lenses out of which 3 were clear, 7 cataracta ferematura and the rest cataracta matura lenses. The optically clear lenses of the 43 and 50 year old persons were also acoustically homo-

geneous. The 63 year old patient's optically almost clear lens was acoustically somewhat heterogeneous. The cataracta ferematura lenses reflected 3-5 echoes but the nuclei were acoustically homogeneous. All cataracta matura lenses were acoustically distinctly heterogeneous and their echograms could be divided into four different groups on the basis of their shape. There was no observable difference in the attenuation of ultrasound caused by clear or opaque lenses.

References

- Baum G. A Synopsis of Ophthalmic Ultrasonography. Wiss. Z. Humboldt Univ. Berlin 14: 51-62 (1965).
- Vet G A & Bronson N R. Ultrasound appearance of senile lens changes. In Ophthalmic ultrasound, ed by Gitter, Keeney, Sarin and Meyer. Pp 218-225. Mosby, Saint Louis 1969.
- Okala A. Über die akustische Struktur der trüben und durchsichtigen Linse. Klin. Mbl. Augenk. 138: 374-380 (1961).
- Okala A & Lehtinen A. Experimental observations on acoustic biomicroscopy of various parts of the eye. Acta Ophthalm. 38: 599-603 (1960).
- Okala A & Varonen E R. The echogram of the normal and opaque lens. Acta Ophthalm. 43: 272-9 (1965).

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THE SYNDROME OF GOLDENHAR AFFECTING TWO SIBLINGS

BY

U KRAUSE

The triad of epibulbar dermoids accessory auricular appendages and pretragal fistulas is termed the Goldenhar syndrome (Goldenhar 1952). This triad is often found in combination with other malformations e.g. hemifacial microsomia coloboma of the upper lids (Sinha & Mishra 1950) ptosis (Proto & Scullica 1966) coloboma of the iris and choroid (Ballantyne 1933) imperforated external auditory meatus (Stallard & Martin 1961) and deafness (Sen Mohan & Gupta 1969). Numerous vertebral column anomalies are common such as occipitalization of the atlas spina bifida spondylolisthesis etc (see Gorlin & Pindborg 1964 Tost 1969). The vertebral bony anomalies tend to be overlooked (e.g. Leiber & Olbrich 1966) but are common and McLusick (1968) uses the term oculo auriculo vertebral dysplasia synonymously with the Goldenhar syndrome. Sabo (1948) describes lipoma conjunctivae in three generations. According to Waardenburg Franceschetti & Klein (1961) there is nothing to indicate that epibulbar dermoids or lipodermoids might be hereditary in man either alone or combined with the syndrome of Goldenhar. Saraux Grignon & Dhermy (1963) describe two affected sisters. Proto & Scullica (1966) three cases of epibulbar dermoids in one and the same family. Since few data are available on heredity in the Goldenhar syndrome it seems desirable to report two siblings thus affected.

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Case reports

Case 1 II/S R L. male born 1960 The proband. Auricular appendages were present bilaterally at birth the midwife tied threads round them and they later fell off. A dark red elevated tumour was seen likewise at birth on the right side of the nape of the neck. The patient therefore entered another hospital in 1963 for the diagnosis Haemangioma nuchae l. dx. The tumour was extirpated the pathologist's diagnosis was hemangioma. At the age of 7 years impaired vision was found in the left eye and the patient now (April 1969) sees an ophthalmologist because the left eye has a peculiar appearance.

Right eye Vision 1/4 refraction +1.5 D. Eyelids were normal. A small flat lipoma like tumour was seen on the conjunctiva close to the lateral angle. There were no hairs on its surface. The cornea was clear the pupil round and responded normally to light. Above, between 11 and 1 o'clock there was indistinct thickening of the iris crypts were lacking but the appearance of the iris was elsewhere normal. The lens was clear a small remnant of the arteria hyaloidea persistens was seen. The papilla and the eye ground were normal.

Left eye Vision 0/9 refraction +1.0 D. Eyelids normal. On the conjunctiva temporally below a small non hairy elevation resembling a lipoma appeared near the corneal border. In this region the conjunctiva was seen to extend for a distance over the cornea which was elsewhere clear. The anterior chamber was of normal depth. The pupil was drawn upward to some extent (Fig. 1) not completely circular and reacted slowly to light. It was somewhat smaller than the right pupil. On retroillumination a defect appeared above in the layer of pigment epithelium the iris stroma extended further out towards the edge of the pupil and showed a partial transition into a greyish membrane. Below a normal iris collarette was visible above this collarette approached the pupillary margin with which it seemed to coincide. The iris tissue was thickened above and normal crypts were not discernible. The vitreous papilla and eye ground were normal.

There were distinct remnants of preauricular appendages in front of both ears (Fig. 9) and on the left a slight indication of a preauricular fistula. No facial asymmetry.



Fig. 1

Left eye of case 1. The iris is thickened above crypts are absent and temporally above, transition of the iris stroma into a membrane is seen at the pupillary margin.



Fig 2 A and B

- I Right eye of case 1 with remnants of pretragal appendices
- II In front of the left ear there is an a remnant indication of a preauricular fistula (arrow)

was observed. On the right side of the nape of the neck there was a scar remaining after hemangioma excision. X ray films showed a normal thoracic spine.

Case 2 II/1 T L a sister of case 1 born 1956. The patient entered our Clinic in March 1968 for extirpation of a conjunctival tumour at the external angle of her left eye. This tumour already present at birth had caused the patient no discomfort. It was excised in local anesthesia. The pathologist's diagnosis was Lipoma. In March 1968 the status was as follows:

Right eye Vision 14 eyelids and conjunctiva were normal and the cornea clear. The iris and the lens as well as the eye ground appeared normal.

Left eye Vision 14 Eyelids were normal. Under the upper lid temporally at the lateral angle there was a lightcoloured slightly prominent tumour. A few hairs were seen on the overlying conjunctiva. The cornea, iris, lens and eye ground were normal. The ears were normal; no preauricular appendages or auricular fistulae were seen. The face was physiologically asymmetrical without demonstrable atrophy.

The presence of two similar anomalies in two siblings led to the examination of other siblings and the parents (Fig 3).

II/2 J L male born 1954. According to the history this was a case of precipitate delivery and the boy weighing 3500 g at birth had neonatal asphyxia. When he was 14 months of age the mother noticed that his right leg was in abnormal position. In 1963 he was operated on for spastic hemiplegia (Allongatio tendinis achillis 1 dx).

Vision bilaterally 14. The conjunctivae and the iris were normal, the lenses clear and the eye grounds showed normal circumstances. The ears were of normal appearance and there was no facial asymmetry. The right leg was 1 cm shorter than the left.

The youngest sibling II/4 J L male born 1964 had an entirely normal ophthalmic

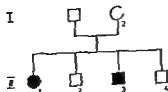


Fig 3

Pedigree of family including two cases of syndrome Goldenhar. All these family members were examined. ■ ● affected member → proband

mological picture. The parents (I/1 and I/2) who were not known to be blood relations did not reveal any findings of special ophthalmological interest.

Discussion

The syndrome of Goldenhar consists of the complete triad of epibulbar dermoids, accessory auricular appendages and pretragal fistulae, but the diagnosis is further substantiated if there are coincidental vertebral anomalies. The multitude of additional symptoms reported make diagnosis more difficult. The presence of incomplete forms of the syndrome has been referred to by Sugar (1966) etc.

The proband showed epibulbar dermoids, preauricular appendages and unilaterally remnants of preauricular fistulae. The diagnosis of the Goldenhar syndrome seems justified in spite of the fact that there was no evidence of vertebral anomalies. The iris anomaly in the left eye was of a type not previously described in connection with this syndrome (see Garner 1951). It is difficult to decide whether the anomaly was primarily neurodermal or mesodermal. The configuration of the iris in the right eye was also pathological and this was evidently a milder form of the same anomaly as affected the left eye.

As seen for instance in the case of the proband, the syndrome displays varying penetrance; for instance the picture differs on the right and the left side. Despite the absence of other anomalies, it is therefore well warranted to regard the sister's (II/1) dermoid as an atypical form of the Goldenhar syndrome and not as a sporadic case of quite another origin. If we accept these conclusions concerning heredity, the question as to the localization and properties of the pathological gene arouses interest. We cannot say anything else with certainty than that the gene is not localized in the X chromosome and that it seems to be of recessive type.

The spastic hemiplegia of one of the brothers had obviously resulted from a

cerebral lesion. This was very likely connected with the precipitate delivery and the postnatal asphyxia. Another possibility is that it was a neurological lesion due to vertebral anomaly such a mechanism would be of interest from the point of view of the pathological changes in the vertebral column seen in the syndrome of Goldenhar. In such a case however the paresis would present a different clinical picture.

Addendum. Besides the proband (II/3) another patient attended our Clinic with the Goldenhar syndrome and cutaneous hemangioma. The patient was a girl of 2 years showing epibulbar dermoids, preauricular appendages, facial asymmetry and a mild left sided macrostomy. In the temporal region there was a hemangioma 1 × 2 cm in size (Fig. 4). A correlation possibly exists between the syndrome of Goldenhar and hemangioma.

Summary

Two cases of the Goldenhar syndrome in a brother and sister are reported. The brother in addition showed anomalies of the iris of a type not hitherto described in this context and also a hemangioma on the nape of the neck. Another brother had spastic hemiplegia probably a result of birth trauma. The correctness of the diagnosis is discussed and the site of the pathological gene dealt with. The possible correlation between syndrome Goldenhar and cutaneous hemangioma is considered.



Fig. 4

Two year old girl with syndrome Goldenhar and hemangioma in the left temporal region

References

- Ballantyne A H A child showing multiple abnormalities Proc. roy Soc Med 1933 6 313
- Garner L L Dermoid of the limbus involving the iris angle and lens Arch Ophthal (Chicago) 1951 46 69
- Goldenhar M Associations malformatives de l'oeil et de l'oreille en particulier le syndrome dermoide epibulbaire - appendices auriculaires - fistula auris congenita et ses relations avec la dysostose mandibulo - faciale J Genet. hum 1952 1 245
- Gorlin R & Pindborg J Syndromes of the head and neck. McGraw Hill New York 1964 419
- Leiber B & Olbrich Gertrud Die klinischen Syndrome Urban & Schwarzenberg Munchen 1966 7:5
- McAusick V 4 Mendelian inheritance in man. Johns Hopkins Baltimore 1968 337
- Proto F & Scullica L Contributo allo studio della ereditarieta dei dermoidi epibulbari Acta Genet. med (Roma) 1966 15 351
- Saba J Lipoma conjunctivae in three generations Acta Ophthal (hbk) 1948 26 447
- Saraux H Grignon J L & Dhermy P A propos d'une observation familiale de Syndrome de Franceschetti Goldenhar Bull Soc Ophthal Fr 1963 63 705
- Sen D & Mohan H & Gupta D K The syndrome of Goldenhar Acta Ophthal (hbk) 1969 4: 1044
- Sinha P Y & Mishra S Corneal dermoid Amer J Ophthal 1950 33 1137
- Stallard H B & Martin P P A case of dermo fibro lipoma of the conjunctiva associated with other congenital abnormalities Brit J Ophthal 1931 15 550
- Sugar S The oculoauriculovertebral dysplasia Syndrome of Goldenhar Amer J Ophthal 1966 60 68
- Tost M Beitrag zur Dysplasia oculo auriculo vertebralis klin Mbl Augenheilk 1969 154 185
- Vaardenburg P J Franceschetti A & Klein D Genetics and Ophthalmog/ Van Gorcum Assen. 1961 volume 1 282

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AN APPENDAGE TO THE OPERATING-TABLE FOR OPHTHALMIC MICROSURGERY

BY

WILLIAM THORBURN

Surgery under an operating microscope is of current interest in ophthalmology. In order to be able to utilize the microscope in the best possible way special arrangement has to be made. The standard operating table does not give the surgeon and his assistant a free and convenient access to the operating field. Therefore the operating table in use was extended by adding an extra appendage. This new table leaf consists of a flat piece of wood which fitted into the tracks of the table otherwise used for the X ray magazines. A horseshoe shaped support for the wrists of the surgeon and his assistant is attached to the leaf around the place where the patient's head rests. The level of the support can easily be regulated and fixed by means of a knob. The support can also be removed thereby allowing the table leaf to be pushed under the operating table. The leaf and the support are covered by a plastic surface and all metal parts are stainless. The leaf is 1350 mm long and 425 mm wide. The horseshoe shaped support is 55 mm wide and slightly rounded and the mean radius of its curvature is 165 mm * See fig 1.

The new table leaf now in use for more than a year has turned out to be of great help. The surgeon and his assistant sit straight across each other in a comfortable position with free space for their knees and easy access to the foot operated control panel.

The operating field can be reached freely from both sides and from above.

Received December 23rd 1969

* This table was manufactured by the workshop of the University hospital Umeå

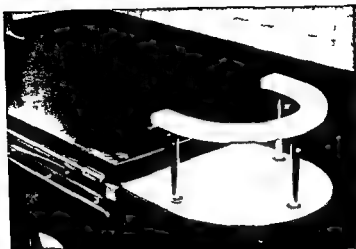


Fig 1

An appendage to the operating table for ophthalmic microsurgery

and the horseshoe shaped support provides a convenient and steady rest for the wrists of the surgeon and his assistant. Furthermore the patients complain much less of breathing difficulties than when usual dressing is used.

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ULTRASOUND (A-MODE) IN A CASE OF NASAL POSTERIOR SCLERAL ECTASY

BY

HANS FLEDELIUS

Posterior staphylomas or scleral ectasies are usually observed in myopic eyes (2). The diffuse myopic stretching and elongation of the weak posterior pole is much more common than the deep sharp-edged staphyloma posticum verum located around the optic disc (12-4).

The depth of the ectasies can be estimated in dioptres by a) direct ophthalmoscopy and retinoscopy (13-10) b) refractometry (3) and c) perimetry (the dioptric value of the lens, which when added before the eye makes the refraction scotoma disappear) (11-8).

Ultrasound presents another possibility of estimating the lesions as reported in two earlier cases (4-14). With the more elaborate B-scan technique the posterior bulbar outline can be reproduced as a soft tissue picture as shown by Trier & Böhm (14) in an excessive myopic patient with bilateral nasal posterior staphylomas and corresponding refraction scotomas. The one-dimensional A-mode ultrasonography makes direct measurement of intraocular distances possible. This method (in the modification of Gernet (5) with optical determination of the anterior segment of the eye) was used in a case of unilateral peripapillary scleral ectasy in a non-myopic eye reported by François et al (4). (The depth of the ectasy was estimated to more than 20 dioptres or 6.07 mm).

Refraction scotomas were not uncommon in a follow-up study of temporal hemianopias published by Riise (9). One of his cases will be reported in more

detail here. The patient presented a unilateral scleral ectasy in the nasal quadrants of an otherwise non myopic eye with normal intraocular pressure. Intraocular distances were determined with A mode ultrasonography which was however made difficult by the peripheral location of the ectasy necessitating an oblique direction of the sound beam.

Case history

A 48 year old female (J No 3393/69-70) had since early childhood been weak sighted in her left eye but she had not otherwise suffered from ocular disease. There was no evidence of squint, myopia or astigmatism in her family.

Eye examination revealed that eye lids, ocular adnexa, eye motility, pupil reactions, intraocular pressure (16 mm Hg both eyes by applanation) and slit lamp examination were normal and the position of the eyes was normal estimated by the cover uncover test.

Right eye

Visual acuity 6/6 + 1.0 sph

Keratometry (Javal Schiotz) $\pm 0.5 D$

Visual field normal by campimetry and Goldmann perimetry

Ophthalmoscopy normal

Ultrasound examination in the assumed optical axis

anterior chamber	3.33 mm
lens	4.14 mm
vitreous	15.03 mm
axis length	22.50 mm

Left eye

Visual acuity $> 6/60 + 2.5 cyl 100$

Keratometry (Javal Schiotz) $\pm 4.0 D$

Visual field: Campimetry showed a defect in the temporal visual field for small white and coloured objects. This was confirmed by Goldmann perimetry (figure 1) which demonstrated the temporal defect for small white objects (II, S) only and not for larger targets (white IV 4).

The defect diminished when concave lenses were placed before the eye and totally disappeared with $-9.0 D$ sph. The ectatic fundus thus achieved better optical conditions and the refractive nature of the scotoma was established.

Ophthalmoscopy: Figure 2 shows the dioptrical estimation of the left fundus achieved with the ophthalmoscopic lenses and confirmed by retinoscopy. The normal macular area was focused with about $+1.0$ sph. On the nasal side of the tilted and normal optic disc with inverse vessel emergence a fundus ectasy was seen with some choroidal atrophy. The maximal depth amounted to about $-1.5 D$ located 5 disc diameters from

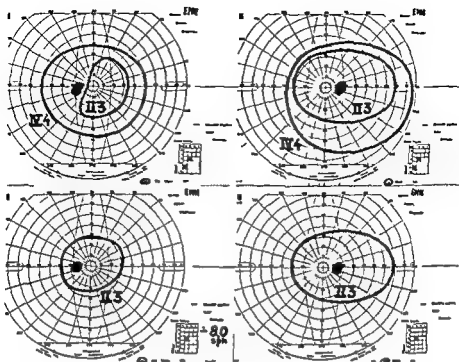


Fig 1

Goldmann perimetry The temporal defect for small white object (II 3) in the left eye (above left) disappears with correction -80 sph (below left) For comparison the isopters of the uncorrected normal right eye (above and below right)

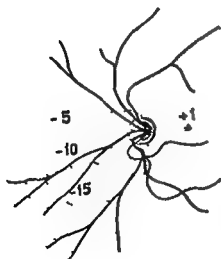


Fig 2

Fig 2 Drawing of the left fundus with the dioptrical evaluation achieved with the ophthalmoscope lenses



Fig 3

Fig 3 The two different positions of the transducer (above) and the directions of the sound beam in the left eye

the optic nerve head. The ectasy was diffuse without sharp demarcation or steep transition to the normal fundus.

Ultrasound examination from top of cornea to macular area (figure 3)

anterior chamber	3.41 mm
lens	4.06 mm
vitreous	15.6 mm
axis length	23.23 mm

Distance from anterior corneal surface to the bottom of the ectasy in the nasal fundus (fig. 3) 27.44 mm. The ectasy itself thus about 4.21 mm.

Ultrasonographic method

Equipment: Kretztechnik Model 7000

The ultrasound measurement procedure grossly followed the outlines of Okala (7) and Jansson (6). A contact glass constructed at Rigshospitalet by D. Ehlers (figure 4) filled with Methocel was interposed between the eye and the ultrasound probe (Ultrasonolux LB 12/PA (1)) making the sound beam traverse a phase homogeneous to sound before entering the eye.

The distances between the echoes from the ocular structures were measured primarily in the potentiometer units of the apparatus. These units were converted to metrical values with an interferometer in an initial calibrating procedure. 100 units corresponded to a passage of sound through 7.346 mm distilled water by 20°C — or through 7.577 mm anterior chamber and vitreous or 8.116 mm lens substance, and these values were used in this study. (The sound velocity in distilled water 20°C is 1486 m/sec in aqueous and vitreous 1532 m/sec and 1641 m/sec in the normal lens (6)).

In this special case however the ordinary procedure could not be followed throughout since the sound beam would hit the bottom of the scleral ectasy perpendicularly only by oblique passage through the lens (fig. 3). The usual



Fig. 4
The contact glass (right) and the Ultrasonolux transducer

high lens echoes – indicating the normally desired visual axis direction of the sound – disappeared by the oblique incidence, and the size of the three separate eye parts could not be obtained. For the conversion of potentiometer units to metrical values we therefore used a theoretical mean value of ultrasound velocity of 1550 m/sec in ocular tissues, assuming a fair balance between the oblique and thereby longer lens passage and the longer vitreous distance due to the ectasy. This mean velocity was calculated from Janssons observations on sound velocities in ocular tissues of women aged 40–49 years (6), and it gave the same total axial length of the ectatic eye (23.23 mm) as the previously mentioned isolated values of anterior chamber lens and vitreous.

Summary

The actual report is the third one in literature on nasal fundus ectasy examined ultrasonographically. The differences from the two earlier published cases (4–14) as regards measurement procedure and anatomical structure have been outlined in the introduction.

The dioptric values of the macular area and the nasal fundus ectasy were estimated to about +1.0 and –1.5 D sph by ophthalmoscopy and retinoscopy. The corresponding bulbar dimensions were 23.23 mm and 27.44 mm determined by A mode ultrasonography. The depth of the ectasy itself thus amounted to about 4.21 mm.

References

- 1 Buschmann W. in Goldberg F. G. & Sarin L. K. *Ultrasonics in Ophthalmology* pp 87–101. Saunders Philadelphia and London 1967.
- 2 Duke Elder S. *System of Ophthalmology* vol VIII Diseases of the outer Eye II pp 998–1003. Kimpton London 1965.
- 3 Jerree C. E. & Rand C. *Arch Ophthalmol* 9: 925–938 1933.
- 4 François J., Goss F. & Yobbagui P. *Ophthalmologica* 154: 446–460 1967.
- 5 Gernet H. *Graefes Arch Ophthalmol* 166: 402–411 1968.
- 6 Jansson F. *Measurements of intraocular distances by ultrasound*. Thesis. Acta Ophthalmol Suppl 74 Copenhagen 1963.
- 7 Oksala A. in Goldberg F. G. & Sarin L. K. *Ultrasonics in Ophthalmology* pp 76–86. Saunders Philadelphia and London 1967.
- 8 Ruse D. *Acta Ophthalmol* 44: 906–918 1966.
- 9 Ruse D. Neuro ophthalmological patients with bitemporal hemianopsia held at the 19th Meeting of Nordic Ophthalmologists in Bergen June 1969. Submitted for publication in Acta Ophthalmol.
- 10 Ronne H. *Klin Mbl Augenheilk* 57: 512–517 1916.

- 11 Schmidt T *Ophthalmologica* 149 250 265 1965
- 12 Sorsby A *Modern Ophthalmology* vol IV p 161 Butterworths London, 1964
- 13 Szlysen A v Augenspiegelstudien zu einer Monographie des Sehnerveneintrittes im menschlichen Auge Wiesbaden 1901 referred by Szly A v *Craefes Arch Ophthal* 110 183 291 1972
- 14 Trier H G & Bohm H W *Diagnostica ultrasonica in Ophthalmologia* pp 263 966 Congress Symposium Brno 1968

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References

1. Buschmann W. in Goldberg E. G. & Sarin L. K. *Ultrasonics in Ophthalmology* pp 87-101. Saunders Philadelphia and London 1967.
2. Duke Elder S. *System of Ophthalmology* vol VIII Diseases of the outer Eye II pp 998-1003. Kimpton London, 1965.
3. Ferree C. E. & Rand C. *Arch Ophthalmol* 9: 925-938 1933.
4. François J., Goes F. & Yobbagui P. *Ophthalmologica* 154: 446-460 1967.
5. Gernert H. *Gracfes Arch Ophthalmol* 166: 402-411 1963.
6. Jansson F. *Measurements of intraocular distances by ultrasound*. Thesis. Acta Ophthalmol. Suppl. 74. Copenhagen 1963.
7. Oksala A. in Goldberg E. G. & Sarin L. K. *Ultrasonics in Ophthalmology* pp 16-86. Saunders Philadelphia and London 1967.
8. Riise D. *Acta Ophthalmol* 44: 906-918 1966.
9. Riise D. Neuro ophthalmological patients with bitemporal hemianopsia held at the 19th Meeting of Nordic Ophthalmologists in Bergen June 1969. Submitted for publication in Acta Ophthalmol.
10. Ronne H. *Klin Mbl Augenheilk* 57: 512-517 1916.

- 11 Schmidt T Ophthalmologica 149 250 265 1965
- 12 Sorsby A Modern Ophthalmology vol IV p 461 Butterworths London 1964
- 13 Silysen A v Augenspiegelstudien zu einer Monographie des Sehnerveneintrittes im menschlichen Auge Wiesbaden 1901 referred by Szly A v Graefes Arch Ophthal 110 183 291 1972
- 14 Trier H G & Bohm H W Diagnostica ultrasonica in Ophthalmologia pp 263 266 Congress Symposium, Brno 1968

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MEDICAL PRESCRIPTIONS FOR CONTACT LENSES

BY

V DREYER

The demand for contact lenses is so heavy that this must be of concern and interest to any ophthalmologist. The *therapeutic* use of the lenses has been generally accepted for many years. The *cosmetic* lenses have to a great extent been discredited, however, it will serve no purpose if the ophthalmologist meets the vain female patient with a sour refusal, since there are too many possibilities of obtaining contact lenses without medical supervision. In cosmetic cases the ophthalmologist should offer "consumer information" with the primary object of pointing out the present medical contra indications against the use of contact lenses. Secondly he should stress the necessity for personal effort on the part of the patient who wishes to become a contact lens wearer and last but not least he must search for a sound motivation, this must be present to counterbalance a fading of the initial enthusiasm. The ophthalmologist is ultimately responsible for the welfare of his patient and it will be he who must cure the epithelial damage caused by wrong lenses. He must master the technique of fitting, since he must be able to point out the errors that have caused a given pathology.

Wearing contact lenses is not completely free of risk. Dixon and his colleagues published in 1966 a study which demonstrated that about one in four thousand of all wearers of contact lenses had lost an eye as a result of complications that could with certainty be attributed to the wearing of contact lenses. Reversible lesions of the eye amounted to 16% in this study. In 1965 Rengstorff showed that out of 100 soldiers wearing contact lenses 99 got foreign

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odies under these lenses during their service period. Furthermore, it was found that 7% of these soldiers lost their lenses in the course of time.

Principles of Fitting

The percentage of success in treatment with contact lenses varies in the available literature. There is hardly any doubt that the number of successful fittings depends upon the method of designing the lenses. In Denmark, Edmund showed in 1967 that for patients who had their lenses fitted by a skilled optician the successes were 54% of all patients who attended the follow-up examination. In Gregersen's study (1967) on weak-sighted contact lens wearers, the lenses were also used adequately in approximately only half the cases. In 1968, Other published a report on aphake patients who had a surprisingly high success rate of 79%.

The two decisive factors for a successful prescription for contact lenses are the cornea's biology and its topography (Stenstrom 1968). Evaluating the corneal biology is a medical task, as it demands a thorough knowledge of physiology, biochemistry, and pathology — topics which are all difficult for a technician to comprehend. The examination of the corneal topography is concerned with optics as well as with medicine. Today, the construction of a contact lens with modifications by stages based on a trial and error method and merely consideration of the fluorescein pattern is only necessary with keratoconus patients and other cases of very irregular corneas. It is true that most current fitting methods include the measurement of the corneal curvature in the visual axis, but this only. The design of the lens is then most often calculated schematically according to an average cornea with a given apical curvature. If we act on average values, we shall be successful in most cases, but this method of procedure has its shortcomings when the corneal topography departs from the average. Furthermore, it is not possible to predict which patients are divergent. There are many standardized lens designs suited for such schematic fittings: there are moulded lenses and turned lenses; there are tri-spheres and lenses with parabolic variation in the peripheral curvature; there are large and small, thick and thin lenses; and there are plastic lenses and gel lenses. Every system has its enthusiastic advocates.

In view of the fact that the topography and biology of the cornea is the most decisive factor in the fitting of contact lenses, and that medical research must adopt the fundamental rule of physics — i.e. to measure all that can be measured and to weigh all that can be weighed — it must be reasonable to make an effort to map out the corneal topography of every individual patient. Several methods have been put forward whose object is the topographic examination

of corneas. The method which in the author's opinion is the quickest and best suited for clinical purposes is the method of *Sampson Soper & Girard*. It is based on the use of the topogometer which was developed in 1964 and this method of fitting has been practised in the present study. The topogometer consists of a fixation light which can be moved in a co-ordinate system with a horizontal and vertical scale on which it is possible to read the size of the area of constant curvature of the cornea – the so called *apical zone*. The topogometer is mounted on the Bausch & Lomb's keratometer which also gives the curvature radius of the cornea in any meridian. Determinations with the topogometer have indicated that the apical zone is often situated eccentrically on the cornea and that the centre of the apical zone – the geometric center of the cornea (i.e. half the distance from limbus to limbus) – and the corneal intersection of the visual axis are by no means always common. As a contact lens cannot be eccentric itself it is necessary to take into consideration any eccentricity of the spherical part of the cornea by allowing the lens to rest eccentrically. *Girard* and his co-workers maintain that the apical zone must wear the contact lens because it is only possible to form a congruence between the two spherical surfaces in this zone.

The question of how a prescribed lens can be tolerated cannot be decided until a suitable period of adaptation has passed. Incomplete information is usually obtained by questioning the patient about his subjective condition only. The acceptance of contact lenses varies individually and it is possible to find a satisfied patient with very serious damage to his epithelium. During the follow-up examination it is necessary to check the visual acuity with the contact lens, the clearance of the lens and the state of the naked cornea after vital stain. The principal rule is to maintain an intact epithelium by all means and to be vigilant against corneal edema. Only in the case of very irregular corneas – mainly with keratoconus patients – can a certain change of the epithelium be accepted.

Before recommending or prescribing the lens it is important to estimate whether in fact it will be of any use to the patient. The advantage of contact lenses in the case of unilateral aphakia has been much discussed. In this discussion it must be stressed that the lenses are conceived as a therapy for aniseikonia and that aniseikonia is of no use unless bifoveal binocular vision is present. Any medical treatment must always be appraised in relation to the disadvantages and advantages of the treatment in question. This is maintained by *Keith Lyle* who in 1953 made an orthoptic study of patients treated for aphakia with contact lenses. He believes that an examination of the binocular vision is of great prognostic importance for the success of the treatment. An orthoptic examination made in advance may reveal whether suppression or diplopia is present or whether artificial hyperphoria due to decentering of the heavy lens will appear. In such cases it is more advisable not to prescribe a contact lens. If suppression is present the contact lens will be to no use and in that case it

would be absurd to expose the patient to the inconvenience and risk which is after all associated with contact lenses. If diplopia is present it must be recognized that being monocular is better than seeing double.

Results

The data presented here arise in part from patients from The Danish Tribunal of Disablement Insurance and in part from patients referred by eye department and private practice. All the patients who had one contact lens only were examined with major amblyoscope. In cases of fusion in a deviating angle only or of small fusional amplitudes the prescription of contact lenses has been rejected to avoid diplopia. This was also the case if suppression was found in the eye that was intended to wear the lens.

Table 1 summarizes all the patients studied. A total of 190 patients have been examined - 58 were primarily rejected for various reasons - 28 did not attend the follow up visit. There remain therefore 89 successful prescriptions where satisfactory fit and power were found and where the lens could be worn continuously for 12 hours at least. Only 16 lenses prescribed by opticians could be accepted - a subject to be dealt with below. The first diagnostic group comprises cosmetic lenses and vocational lenses. Here a considerable absenteeism is noticed when the follow up examination became due and the reason for this probably was that some patients had abandoned their intention of getting contact lenses as a result of the information as to inconvenience and the risk involved at the first examination. The largest group of prescriptions is found in disabling myopia which is here defined as a myopia exceeding 7 diopters. A number of patients in the group of degenerative myopia were rejected because it was impossible to improve a visual deficiency caused by major central degenerations. The group of monocular aphakia represents the largest number of applicants. However it is also the group where most patients were dissuaded at the outset from wearing contact lenses because of predominant chances of disorganization of binocular function. A relatively large number were fitted with contact lenses for bilateral aphakia - in this group the success has benefited from the fact that the patients are often old with a corresponding decrease of the corneal sensibility.

Contact lenses are not the only way of treating keratoconus. In these respects the degree of this disease can be subgrouped as follows: 1) the mild group where ordinary spectacle glasses are adequate, 2) medium - severe group that has great advantage from the use of contact lenses and 3) the most severe group where keratoplasty will be necessary (Gjard & Soper 1965). As shown in the table a fairly large number of patients in the keratoconus group were primarily

Table 1
190 examined patients – grouped according to diagnosis

	Total	Primarily rejected	Absentees	Medical prescript	Approved technician fits
Vocational and cosmetic lenses	32	6	12	14	0
Medical indications					
High myopia	24	4	2	17	1
Degenerative myopia	21	7	3	10	1
Monolateral aphakia	69	31	6	24	8
Bilateral aphakia	19	3	2	12	2
Keratoconus	11	6	1	4	0
High degree astigmatism	5	0	1	2	2
Keratoplasty	5	1	1	2	1
Neuroparalytic keratitis	2	0	0	2	0
Corneal scars without aphakia	2	0	0	1	1
	190	58	28	88	16

rejected because good vision could be obtained by means of ordinary glasses. However, continued follow up examinations have been offered these patients and some of them must be expected to change to contact lenses later. Other corneal irregularities such as high astigmatism, the sequelae of keratoplasty, neuroparalytic keratitis with damaged corneal epithelium and finally corneal scars are rare indications but such patients have also proved well suited for contact lenses.

Table 2 indicates the most important causes of rejection. This shows that in the entire material deficient binocular sight is also the main cause of refusal – comprising about half the number of patients. One third was rejected because no improvement of vision could be achieved because of opaque media or retinal degenerations. Finally a minor group was rejected because of contraindicating eye diseases such as an angle closure glaucoma, recidivating herpetic keratitis or vigorous blepharitis which were considered to make the possibility

Table 2
Primary reasons of rejection

Deficient binocular vision	52%
No improvement of acuity	32%
Former or foreseen wearing difficulties	16%

of wearing contact lenses doubtful. A very small number were rejected because of difficulties already demonstrated in wearing correct contact lenses. This minor group comprises mainly cosmetic cases with weak motivation.

Table 3 gives the findings in 94 patients who came to the examination with lenses fitted by technicians. In most cases there had been no efficient ophthalmological survey. These patients were examined because subjective and objective signs of maladjusted lenses were reported. This may explain the fact of only 18 per cent acceptance. However, the selection shows that a contact lens fitted by a technician exclusively can scarcely *a priori* be trusted to be correct.

On evaluation of the lenses already delivered, visual acuity with the lenses, the motility and clearance of the lens and epithelial state after vital staining without lens have been evaluated. Strangely enough, the error most frequently noticed was attributable to the power of the lens: nearly half of the lenses presented were of the wrong power. The reason may be an imperfect technique of refraction, but the most probable reason is that the first refraction made by the technician with the trial lens is done without the use of anaesthesia of the cornea - thus making the refraction laborious because of an overflow of tears and irritation. Damage to the epithelium was observed in one third of the cases and excessive movements in one quarter of the cases.

Table 3
Optician's prescription.

Number of patients examined	94 = 100%
Number of lenses to be modified	77 = 82%
Number of accepted lenses	17 = 18%
Reasons for modifications	
Incorrect power	48%
Damage to the epithelium	30%
Lens lag or too large excursions	2%

Table 4 gives an outline of 116 prescriptions carried out at the clinic on basis of a topogometer examination and refraction with trial lens. Approximately half the patients had no previous experience in wearing lenses and the other half were advised on the modification of a prior prescription. Only two patients (about 2 %) had to discontinue wearing contact lenses. The successful fittings can be made out 76 % but in fact the actual percentage must be well over 80 since it is believed that some of the absent patients were actually successful in wearing contact lenses. This opinion was confirmed by a number of calls from the patients or their opticians. The "successful prescription" criterion does not consider whether the patient later used the lenses after an arbitrary period of observation. The criterion of actually being able to wear the lenses during all working hours without damaging the cornea must be the medically important factor and the contact lens should not be blamed if a few patients later give up wearing them for personal reasons.

Table 5 shows the distribution of age and sex among the 88 successful prescriptions. There are more women than men and an accumulation according to age in the decades of 21-30 years (the myopias) and 51-60 years (the aphakias). Table 6 shows the need for modification of the originally prescribed lens in 88 successful prescriptions. 61 % of the patients needed only one prescription and after becoming accustomed they could wear the lens all day. In 30 per cent one modification was necessary. It was often necessary to alter the over all diameter or the intermediate posterior curve but in rare cases the central posterior curve. In 9 % more than two modifications were necessary. The need for modifications was equal in novices and in former wearers.

Table 7 lists the over all diameters prescribed. We find that *Girard's* fitting method results in fairly small lenses and that the predominating diameter is about 9 mm. From the table we can also conclude that omitting the measure

Table 4
116 prescribed contact lenses

No prior prescription	63
Re prescription because of imperfect lens from an optician	33
Total	116
Absentees from follow up visits	26
Discontinued during period of adaptation	2
	99
No follow up as a percentage of total prescriptions 24 %	
Number of subjects to be reviewed	88

Table 5
88 successful prescriptions

Age	Number	Men	Women
<10 years	2	1	1
10-20 years	13	5	8
21-30 years	26	11	15
31-40 years	12	5	7
41-50 years	11	6	5
51-60 years	16	7	9
61-70 years	6	2	4
> 70 years	2	1	1
	88	38	50

Table 6
88 successful prescriptions for contact lenses

	New CL pts	Former CL pts	Total	Per cent
First design satisfactory	28	26	54	61
One modification necessary	14	11	25	30
More modifications necessary	7	1	8	9
	49	38	87	100

Table 7
Prescribed lens diameter

60-70 mm	7%
80-99 mm	80%
100-119 mm	13%

ment of the apical zone and operating instead with a standard lens diameter must in all cases have the consequence that about 20 % of all the prescriptions will not result in correct diameters

Table 8 sums up the prescribed central curvatures. Here an accumulation is found in the 42.0 D-43.9 D groups. It can similarly be concluded that if a posterior curve of about 43 D (or a little below 8 mm) were used as a standard the consequence would be that only a little below half the cases would have turned out successfully.

Summary and Conclusion

The data here presented emphasize 1) that it is possible for an ophthalmologist to fit contact lenses satisfactorily as regards wearing period, visual acuity and corneal adaptation without too much time-consuming effort. In more than half the cases the visits have not lasted more than 1½ hours in all.

2) that an initial selection of patients suited for contact lenses results in a success percentage that is way above the averages mentioned in literature.

3) that an examination of the corneal topography is necessary to obtain a high percentage of success.

4) that close cooperation between ophthalmologist and technician is necessary.

5) that it must be the ophthalmologist who directs the treatment and that he must know the fitting technique so well that he will be able to discuss necessary modifications if any.

6) that future research and improvement of contact lenses is supposed to reach the optimum results if treatment is centralized preferably at hospital centers which employ contact lens opticians.

Table 8
Prescribed posterior central curves

40.0-41.0 D	28 %
42.0-43.9 D	47 %
44.0-45.9 D	19 %
46.0-47.9 D	4 %
48.0-49.9 D	0 %
50.0 D	2 %

References

- 1 Dixon J M Am. J Ophth 1967 58 474
- 2 Edmund J Ugeskr f Læger 1967 196 916
- 3 Girard L J (ed) Corneal Contact Lenses Mosby St. Louis 1961 p 81
- 4 Girard L J & Soper J W Ophthalm 1965 100 161
- 5 Gregersen F Acta Ophthal 1967 45 119
- 6 Lyle T K Trans Ophthal Soc U K 1953 73 387
- 7 Rengstorff R H Milit Med 1965 130 419

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INCIDENCE OF CILIORETINAL ARTERIES

BY

S E LORENTZEN

A cilioretinal artery is a terminal artery like the retinal branches from the central retinal artery. Presence of a cilioretinal artery involves that dependent on the size of this a larger or smaller region of the retina receives its blood supply *via* the posterior ciliary arteries with no relation to the central retinal artery. This may become of practical importance in two situations. One is that of total occlusion of the central retinal artery with an at the same time functioning cilioretinal artery and the other that of an isolated occlusion of a fairly large cilioretinal artery.

At total occlusion of the central retinal artery a functioning cilioretinal artery can maintain the blood supply to the retinal region involved. As this region often includes the macula a normal central vision may be preserved of an eye affected by total occlusion of the central retinal artery. This is a clinical picture reported several times in the literature since the end of the 19th century. It occurs so frequently and is so well known among clinicians that simple cases are no longer published. In a series of 37 patients with occlusion of the central retinal artery (Lorentzen 1969) one had a functioning cilioretinal artery. A special case of this kind was reported by Andrzejewska (1967) seen in a patient with macular degeneration of the right eye and a central artery occlusion of the left. In the left eye a functioning cilioretinal artery secured the central vision and supplemented the visual field of the right eye thereby enabling the patient to work and move freely about.

Isolated occlusion of a cilioretinal artery was first described by Hirsch in 1896. Since another 14 such cases have been reported of which 13 are known from quotations by Hayreh (1963) while Gandolfs (1946) described one case. An account of a fifteenth case is due to Ferre, De Oliveira & Alterman (1967).

Table I gives a survey of the incidences of cilioretinal artery noted previously on the basis of ophthalmoscopy.

Material and Results

The total series comprised 112 healthy subjects: 63 males and 104 females ranging in age from 10 to 19. They were subjected to out-patient examination. The majority were examined with a view to refractive anomalies while in some cases the examination constituted part of a general examination. The series included none with ophthalmologic abnormalities nor any with fairly pronounced abnormalities of refraction (refraction between + and - 3 D). Direct ophthalmoscopy was performed using a powerful electric ophthalmoscope. The series is identical with one employed previously for studying the incidence of spontaneous venous pulsation in the retina (Lorent in 1970).

Only arterioles having the following ophthalmoscopic characteristics were included as cilioretinal arteries. The arteriole turns up at or just within the disc margin and proceeds towards the middle of the disc. It then continues crossing the disc margin outwards in the retina running a more or less straight course like any other retinal arteriole. Thus along the first part of its course the arteriole forms a hook which has been compared to the handle of a walking stick.

Table II shows the number of examined subjects grouped according to sex and the number of discs left and right respectively with cilioretinal artery.

In 45 or 40 per cent of the 112 examined subjects one or two cilioretinal arteries were found. In 7 or 6 per cent, of the 112 a cilioretinal arteriole was seen on each disc. Of the 344 examined eyes 52 (15 per cent) had cilioretinal arteriole on the optic disc. Five (9.6 per cent) of these 52 discs presented two cilioretinal arterioles on the same disc the remaining 47 only one.

Table III illustrates the quadrantal location of the cilioretinal arteriole on the disc. In table IV the cilioretinal arteries have been grouped according to size. Only half of the observed cilioretinal arterioles were large enough to be of practical importance with regard to the blood supply of the retina. Nearly all the large cilioretinal arterioles were found to play a functional role: 94 per cent supplying the posterior pole and often also the macular region by virtue of their temporal origin on the disc.

Table I
Survey of reported incidences of cilioretinal arteriole and author's own observations

Author	Number of subjects examined	Number of eyes examined	Number of eyes with cilioretinal artery	% of eyes with cilioretinal artery	Number of subjects with cilioretinal artery	% of exam with cilioretinal artery	Number examined w/ bilat cilioret artery	% of examined w/ bilat cilioret artery	% of subjects w/ cilioretinal artery having such bilaterally
Randall 1887	Not stated		about 20 %						
Lang & Barrett 1889		48	8	16.7 %					
Elshing 1897	170	340		about 7 %					
Jackson 1911	500	1000	191	19.1 %	148	29.6 %	43	8.6 %	29.0 %
Salzmänn 1912	Not stated			17 %					
Jensen 1936	100	200	16	8 %					
Bullwinkel 1934	ab 500	ab 1000		16 %					
Mann 1957	Not stated			>25 %					
Collier 1957	1000	2000	250	12.5 %	216	21.6 %	34	3.4 %	15.7 %
Mehra 1965	1448	2896	117	4.0 %	100	6.9 %	17	1.2 %	17 %
Lorentzen 1970	172	344	32	15 %	4	26 %	7	4.1 %	1.5 %

Table II

The table shows number examined number examined with cilioretinal arterioles and percentage frequency of such grouped according to sex and laterality The bracketed figures indicate the numbers of discs with two cilioretinal arterioles

	Number examined	Number with cilioretinal artery			Number examined w cilioretinal artery	% of examined with cilioretinal artery
		Right	Left	Bilateral		
Males	68	7 (1)	5		12	18 %
Females	104	16 (1)	10 (2)	7 (1)	33	32 %
Males + Females	172	23 (2)	15 (2)	7 (1)	45	26 %
Eyes	344	93 (2)	15 (2)	14 (1)	52	15 %

Table III

Quadrantal locations of 57 cilioretinal arterioles in 45 subjects Seven bilateral Five discs each presented two cilioretinal arterioles (bracketed figures)

Quadrant	Number	%
Upper temporal	21 (2)	40
Lower temporal	28 (3)	54
Upper nasal	2	4
Lower nasal	1	2
All	52 (5)	100

Comments

The incidences of cilioretinal arteries arrived at in the present study namely 15 per cent of examined eyes and 26 per cent of examined subjects correspond to the values given in the literature Jackson (1911) found cilioretinal arterioles in 19 per cent of examined eyes and 29.6 per cent of examined individuals Bullwinkel (1954) in 16 per cent of examined eyes and Collier (1951) in 12.5 and 21.6 per cent of examined eyes and examined individuals respectively

It is worth noting however that in no more than about half of the cases are the cilioretinal arterioles of such a size that the retinal region supplied by them

Table IV

Distribution according to size of 57 cilioretinal arterioles in 52 eyes of 45 subjects
 Large = extending two disc diameters or more (for temporal arteriole to macula or further) from the optic disc

Medium = extending between one and two disc diameters from the optic disc.

Small = extending less than one disc diameter from the optic disc

	Right eye	Left eye	Bilateral	All
Large	9	9	4 + 6	28
Medium	13	4	2 + 1	20
Small	3	4	1 + 1	9
All	25	17	7 + 8	51

has any functional influence on the vision. This is probably one of the reasons why an isolated occlusion of a cilioretinal arteriole has comparatively rarely been reported in the literature. Such an occlusion of a fairly small cilioretinal arteriole may occur without being noticed. Another possible cause of the infrequent publication of reports on isolated occlusion of a cilioretinal arteriole is the fact that occlusions of cilioretinal arterioles as such are rarer phenomena than occlusions of the central retinal artery and its branches.

Hayreh (1963) pointed out that we cannot definitely conclude that any arteriole located peripherally on the optic disc is a cilioretinal arteriole. It may be an early ramification from the central retinal artery. However, Elschnig as early as 1897 showed histologically in 13 cases that arterioles having the ophthalmoscopic characteristics employed in the present study were direct or in direct branches from Zinn's circle, in other words originating from the posterior ciliary artery.

Cilioretinal arterioles most often make their exit from the temporal disc margin, almost equally often from the upper and the lower quadrant. In the series under review the cilioretinal arteriole was located temporally in 94 per cent and nasally in 11 per cent. Of Jackson's (1911) 191 eyes 188 had the cilioretinal arterioles temporally on the disc. Collier (1957) found temporal location in 81 per cent and nasal in 13 per cent.

In the present series the phenomenon was seen in 23 right eyes (60 per cent of right plus left) and in 15 left eyes (40 per cent of right plus left). Collier (1957) found the reverse distribution. Jackson (1911) observed 53 right and 52 left. Thus the two eyes seem not to differ with regard to frequency of cilioretinal arterioles.

Five discs each showed two cilioretinal arterioles. Among these was one disc of one of the seven subjects with bilateral cilioretinal arterioles. Jackson (1911) among 191 eyes with cilioretinal arterioles found 12 discs with two such arterioles and two with three.

Summary

The incidence of cilioretinal arterioles has been studied in a normal series comprising 112 subjects (68 males and 104 females) ranging in age from 10 to 19. Cilioretinal arterioles were found in 45 of the subjects (26 per cent) and 52 of the eyes (15 per cent). These were unilaterally present in 38 subjects and bilaterally in seven. Five of the 52 discs presented two cilioretinal arterioles while the remaining 47 discs had only one each. 94 per cent of the cilioretinal arterioles made their exit from the temporal quadrants of the disc. Only about half of the cilioretinal arterioles are of a size to make the retinal region they supply play a role with regard to the visual function.

Mention is made of the significance of cilioretinal arterioles.

References

- Andrzejaska W. Szerególny przypadek uzupełniania się patologicznych pol widzenia obu oczu. Klin. Oczna 1967 37 111-114. Cited after Excerpt Med. XII 1967 21 No 71.
- Fullenkett H. C. Cilioretinal vessels. New York State Journ. Med. 1934 54 1462-1463.
- Gillier Michel. Frequence des vaisseaux cilio-retiniens leur rapport avec les anisotropes leur association avec d'autres anomalies du fond de l'oeil. Bull. Soc. Ophthal. France 13 35-60.
- Ellis haig Anton. Cilioretinale Gefasse v. Graefes Arch. Ophthal. 1897 44 144-171.
- Fernandes De Oliveira L. V. & Herman H. A. A proposito da oclusao de uma arteria cilio-retiniana. Arq. Inst. Ocul. 196 12 133-144. Cited after Excerpt Med. XII 1966 No 70-3.
- Fould H. C. Importanza delle arterie cilio-retiniche nelle lesioni circolatorie della retina. Ann. Ocul. 1946 446. Cited after Excerpt Med. XII 1948 No 142.
- Hayter S. F. & Singh G. The cilio-retinal arteries. Brit. J. Ophthal. 1963 46 11-19.
- Helmholtz H. Zur Pathologie der Embolie der Netzhautschlagader. Arch. Augenheilk. 1884 33 141-155.
- Jackson E. F. & Cal. retinal and other anomalous retinal vessels. Ophthal. Rev. 1911 10 64-74.
- Jackson E. F. Clinical studies of tributary thrombosis in the central retinal vein. Arch. Ophthal. 1906 Suppl. 2.

- Lang W & Barret James W* On the frequency of cilio retinal vessels and of pulsating veins London Ophthal Hosp Rep 1889 12 59 60
- Lorent en S E* Occlusion of the central retinal artery A follow up Acta Ophthal 1969 47 690 703
- Lorent en S E* Incidence of spontaneous venous pulsation in the retina Acta Ophthal 1970 48
- Mann Ida* Developmental abnormalities of the eye 2 ed British Med Assoc London 1957
- Mehra Krishna Swami* Incidence of cilio retinal artery in Indians Brit J Ophthal 1965 49 52 53
- Randall B Alex* Cilio retinal or aberrant vessels Trans Amer Ophthal Soc 1887 4 511 517
- Sal mann Maximilian* The anatomy and histology of the human eyeball in the normal state Its development and senescence Transl by E V L Brown Chicago 1919 p 183

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FOCAL DERMAL HYPOPLASIA

Ocular and General Manifestations With a Survey of the Literature

BY

METTE WARBURG

In an institution for the mentally retarded I have seen a case of focal dermal hypoplasia (FDH) a syndrome of which 32 cases have been published previously none so far in the ophthalmological literature

Case History

The patient was a 38 year old severely retarded blind and deaf woman. She was the last born of 8 siblings and had no known family history of skin or mental diseases. Birth was 9 weeks prematurely and birth weight 2000 g (5½ lbs). She had a congenital skin condition which was interpreted as amniotic adhesions. During the first year of life an examination (University Eye Clinic, Copenhagen) showed congenital nystagmus, clear corneae, microphthalmia, symmetrical colobomata of the irides and ectopia of both lenses. A supernumerary finger was removed from the ulnar side of the right fifth finger at age 17.

Until age 9 she was able to walk, she then sustained a fracture of the femur and has since been confined to bed.

Hearing was good until age 15 when recurrent discharge occurred due to

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- Lorent en S E* Occlusion of the central retinal artery A follow up Acta Ophthal 1969 47 690 703
- Lorent.en S E* Incidence of spontaneous venous pulsation in the retina Acta Ophthal. 1970 48
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General condition She was 126 cm (4 feet 1/4 inches) high and weighed 19.5 kg (43 lbs) The skull was microcephalic the nose pointed and deviating to the left The teeth were absent the palate flat and the chin well developed Granulomata were present in the external auditory meatus on both sides and a post operative fistula behind the left ear communicated with the middle ear Hearing was presumably absent There was contracture of both sterno cleido mastoid muscles which produced a head tilt towards the left shoulder The neck was short and there was a cervical scoliosis A monstrous dextro convex kyphoscoliosis was present in the dorsal region the left curvature was approximately 7 centimetres below the iliac crest (Fig 2)

Both breasts were poorly developed and a supernumerary nipple was found on the right breast near the anterior axillary fold No pubic or axillary hair was present The anus was anteriorly displaced the clitoris was absent and the labia majora and minora were very small Scanty menstruation occurred regularly

Skin The skin of entire body was thin dry and scaling It presented numerous small white areas and many brownish patches There were herniations of subcutaneous fat on both calves

Scratch mark was seen everywhere The hair was scanty and almost absent at the vertex of the scalp but it was not worn off in the nuchal region The lips

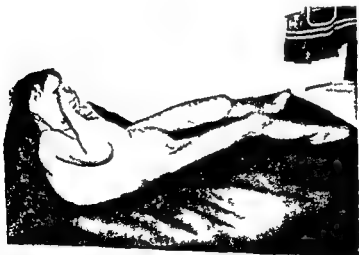


Fig 2

Dx: ad kyphosis in patient with focal dermal hypoplasia. Telangiectases and patchy pigmentation can be seen on the back and legs Note absence of pubic hair

papillomata in both external auditory meatuses and middle ears. Papillomata also occurred when aged 23 on the left labium major and in the coccygeal region. They did not recur after curettage. The teeth had always been small and deeply set in the gums. They were lost at an early age. Mentally she was always severely retarded and never learnt to talk. She was seen at age 31 and 38 and the findings were identical.

Examination (Case rec 1/69)

Eyes There was no perception of light. Both eyes were small and deeply set. The diameter of the right cornea was 5 mm, the left 4 mm. Horizontal and vertical nystagmoid movements were present. Both corneae showed extensive opacities without vascular invasion. In the right eye a more translucent area of approximately 1 mm enabled the observation of a white cataract (Fig 1).



Fig 1

Face of patient with focal dermal hypoplasia syndrome. The eyes are microphthalmic, the corneae clouded. The nose is pointed and deviating; the skin of the lips is particularly dry. Pigmentations are seen on the breast.



Fig 4
X ray of feet.

Discussion

17 cases of IDH have been reported previously. The name was coined by Golt *et al* (1962) and Gorlin *et al* (1963) found 12 previously reported cases - described under different names. Since 1963 ten further cases have been published. A survey of these and other cases found in the literature is presented in Table 1. Table 2 is a survey of the principal features of the disease. Congenital dysplasia of the skin and extremities are obligate signs of the condition. This of course may be a biased point of view as nearly all case histories have been reported by dermatologists. At birth the skin shows scattered lipoma like lesions and atrophic areas which sometimes ulcerate and finally heal by scarring. The lesions do not change much during life. Focal areas of thin atrophic skin interspersed by telangiectasies or pigmented streaks are seen all over the body and the extremities. The lipoma like areas are small reddish yellow or white herniations of subcutaneous fat protruding through defects of the dermis. It is common for the affected persons to have papillomata at the mucous membranes

were particularly dry and scaling but papillomata were present only in the ears. The patient was capable of sweating.

Extremities The patient kept her elbows flexed and her hands in front of her chest but there were no contractures in the arms or legs apart from the hip joints which could not be extended. The right hand showed a cutaneous syndactyly between the third and fourth finger. The right foot showed syndactyly between the second and third toe and the fifth toe originated 3 centimetres proximally to the other toes. The nail was absent on this toe. The left foot was a cleft foot with a rudimentary toe on the medial side of the third toe (Figs 3a, 3b, 4).

Laboratory investigations demonstrated nothing abnormal. Paperchromatography of amino acids in urine and serum showed no significant deviations from normal (Professor Lundquist, The Biochemical Institute, University of Copenhagen) and the karyogram showed a normal karyotype 46/XX (M. Mikelsen, M.D., University Institute of Human Genetics, Copenhagen).



Fig 3

Feet of patient with focal dermal hypoplasia. Left foot is split and consists of only three toes. There is syndactyly between the second and third toe on the right foot and the third and fourth of the left foot.



Fig 1
X ray of feet

Discussion

11 cases of FDIH have been reported previously. The name was coined by Golt *et al* (1967) and Gorlin *et al* (1963) found 12 previously reported cases - described under different names. Since 1963 ten further cases have been published. A survey of these and other cases found in the literature is presented in Table 1. Table 2 is a survey of the principal features of the disease. Congenital dysplasia of the skin and extremities are obligate signs of the condition. This of course may be a biased point of view as nearly all case histories have been reported by dermatologists. At birth the skin shows scattered lipoma like lesions and atrophic areas which sometimes ulcerate and finally heal by scarring. The lesions do not change much during life. Focal areas of thin atrophic skin interspersed by telangiectasies or pigmented streaks are seen all over the body and the extremities. The lipoma like areas are small reddish yellow or white herniations of subcutaneous fat protruding through defects of the dermis. It is common for the affected persons to have papillomata at the mucous membranes

Table 1
Survey of previously reported cases of focal dermal hypoplasia

Authors	1	2	3	4	5	6	7	8	9
Kruger 1917	M	+			+				
Jessner 1921	F	+			+				
Naegeli 1927	F	+			+				
Jessner 1929	M	+		C	+		R		
Marchionini 1932	F	+		S	+				
Liebertmann 1935	F	+	+	PS	+				
Cole 1941	F	+	+		+				
Hulley 1941	F	+	+	SA	—		N	T T S	+
Wilson 1952	F	+	(+)	A					
Gold 1958	F	+		SA	+			S	+
Callagher 1953	F	+				C	MR	T	
Freeman 1955	F	+		S					
Nickel 1956	F	+		A		C	M	ST	+
Mankopf 1957	F	+	+			C	N		
Wodnianski 1957	F	+		SA			M		
Becker 1955	F	+		SA		CM	M	S BT	+
Rook 1959	F	+		S		C			+
Holtinger 1961	F	+	(+)						+
Goltz 1963	F	+		P	+	C	HR		+
Gorlin 1963	F	+	+						
Mieczniki 1963	F	+	+	SC	+	CMO	MR	T	+
Solomon 1963	F	+	(+)	SP	+	C	N		+
	F	+	+	S	+	CMO	N	(T)	+

Table 2
Symptoms of reported cases of focal dermal hypoplasia

	Sex	Skin	Phalanges & Metacarpals	Eye	Teeth	CNS	Spine
Sex distribution	29F/3M						
Focal atrophy & pigmentations		33					
Nail dystrophy		21					
Papillomata		17					
Typical histology		15					
Syndactyly			21				
Metacarp /Phal aplasia/hypoplasia			11				
Polydactyly			4				
Cleft hand/Foot			3				
Coloboma				11			
Microphthalmia				5			
Optic atrophy				1			
Ectopia of lens				2			
Abnormal teeth					12		
Microcephaly						6	
Mental retardation						7	
Scoliosis							5
Spina bifida							3

of the mouth the orifice of the external auditory canal the anus and the vagina The nails are thin brittle deformed or wholly or partially absent The teeth are small and often fall out at an early age

The skeletal defects may vary from insignificant shortening of a metacarpus or presence of camptodactyly but are usually severe presenting aplasia or hypoplasia of fingers or toes lobster claw hands or feet syndactyly or polydactyly Scoliosis is not uncommon and microcephalus has been noted

Malformations of the eye have been frequently reported Apart from the trivial sign of squint colobomata have been found in 11 cases and microphthalmia has been noted in 5 cases Optic atrophy aniridia and ectopia of the lens are on record as well

Microscopic examination of the skin from atrophic areas shows a normal epi

dermis and subcutis while there is a nearly total absence of the dermis to the effect that the subcutaneous fat is situated just below the surface of the skin. Elastic fibres are degenerated. In the papillomatous areas the epidermis is hyperkeratotic and hyperplastic.

Of the 32 cases found in the literature 28 occurred in females

Differential Diagnosis

Holden (1961) probably was right when he said that the FDH syndrome is so striking that there is little confusion with other entities before the syndrome was delimited out as a separate entity it was confused with *Rothmund Thomsen's* disease which also show atrophic skin and telangiectasies. In this disease the hands and feet are often small but there are no skeletal malformations. It shows a certain affinity to women but 30 % of the cases reported have occurred in males. In contrast to the FDH syndrome *Rothmund Thomsen's* disease is not congenital. It appears at the age of 3-6 months with an initial erythema. The eyes often show cataract and colobomata are not seen.

Incontinentia pigmenti (Bloch Sulzberger) also sometimes present focal atrophies of the skin (*Holtzinger* 1961). The disease is congenital but the initial lesions are vesicles and bullae which eventually are transformed into pigmented maculae. These fade during later years. The hair may be scanty and defects of teeth and nails have been reported. All affected are females. The eyes have not shown microphthalmia or colobomata but may present pseudogliomatous lesions. Skeletal anomalies are not part of this syndrome.

Xanthus lipomatosus superficialis (Hoffmann Zurhille) is a congenital skin lesion with hyperplasia of the subcutaneous fat which gives rise to congenital papules under the skin. There are no other malformations associated with this syndrome.

Progeria is another disease presenting a few months after birth. The affected persons are of small stature the skin is atrophic and there is atrophy of subcutis and muscles. The hair is thin and alopecia is frequent. Teeth and nails are dysplastic. The skin lesions are diffuse and not focal there are no skeletal malformations and according to Waardenburg microphthalmia and colobomata are not a part of this syndrome.

Cockayne's syndrome sets in during the first few months of life. The skin is particularly sensitive to light and traumata and soon presents small localised pigmentations and scars. Anhidrosis and dwarfism is common. Skeletal malformations do not occur. Deafness and blindness due to retinitis pigmentosa are characteristic features and colobomata or microphthalmia do not occur.

Congenital stippled epiphyse (*Conradi's disease*) is associated with con

genital patchy erythema in the head and scalp (*Comings et al* 1961). Few affected persons survive but in these the skin shows cicatricial alopecia and follicular atrophoderma. The epiphyseal stippling eventually disappears and scoliosis becomes apparent during childhood. Cataract has been noted during infancy.

Aetiology

It is as yet unknown if FDH is caused by a teratologically active agent or is a genetically determined trait. Major chromosomal anomalies can be disregarded as several examinations have shown normal karyotypes. It is significant that all but two of the reported 32 cases have occurred in females and *Gorlin et al* (1963) reported a mother of an affected girl to have minor symptoms of the disease. Most of the patients published have been children and women with the florid syndrome have not been known to give birth to children. Their unfortunate appearance may account for a selective disadvantage. Further *Gorlin* points out (personal communication) that the reproductive organs of the affected women are often infantile. It has been maintained that there is an overrepresentation of abortions in the sibs of the affected patients. If a genetical mutation is responsible for the disease it would on the basis of the severe structural anomalies present be supposed to be a dominant one (*McKusick* 1966) and the genetical problems presented by the FDH syndrome would be the same as those of incontinentia pigmenti, the oro-facial digital syndrome, the Wilder-vanek syndrome and some hereditary cases of congenital cataract with microphthalmia, all of which are limited to females.

In this syndrome a multitude of theories have been put forward including autosomal dominant heredity with sex limitation (*Gorlin et al* 1963), sex-linked dominance with lethality in the males (*Wahrmann et al* 1966 in a case of oro-facial digital syndrome occurring in an $47/X\text{-}X\text{-}Y$ male), transmission of cytoplasmic inclusions (*Shott & Emery* 1966) or gene duplication as suggested by *Jones et al* (1967) in thyroxine binding globulin of serum.

After this paper was completed *Golt et al* (1970) reported typical cases of focal dermal hypoplasia in two girls, one with monolateral coloboma of the iris and choroid.

Summary

The 33rd case of focal dermal hypoplasia is reported. The patient was a severely retarded blind and deaf woman aged 38 years. She presented focal atrophies

pigmentations telangiectases of the skin and fat herniations. The secondary sex characters were poorly developed. There was a monstrous dorsal kyphosis, lobster claw foot and other malformations of the hands and feet. The eyes were microphthalmic with bilateral colobomata of the irides and ectopia of both lenses. A survey of previously reported cases and a differential diagnostic discussion is given. Aetiological considerations are similar to those presented by incontinentia pigmenti, the orofacial digital syndrome, the Wilder-Ranck syndrome and certain hereditary cases of congenital cataract and microphthalmia which all are restricted to females.

Key words: Focal dermal hypoplasia, microphthalmia, malformations of the eye, malformations of the skeleton, mental retardation.

References

- Barta L. & J. Lengyel: Über ein Syndrom mit naeviformen Hautatrophien (Systematisierte naeviforme Atrophodermie). *Ann paediat* 90: 235 1966.
- Becker S. W. & D. G. Lindsay: A case for diagnosis: Thomson's poikiloderma. Ectoderm I and mesodermal dysplasia with osseous involvement (Croteau et al.). *Rothmund's syndrome?* *Arch Derm* 120: 1258.
- Braun-Falco A. & S. Margheciu: Über eine systematisierte naeviforme Atrophodermie. *Arch klin. & Exper Derm* 91: 549 1965.
- Callaert E. J. M. E. MacGregor & M. Israeliki: Chondrodystrophy with ectodermal defects. *Arch Dis Child* 48: 14 1973.
- Cusido A. M. C. Bianchi O. Bianchi I. Mutante & R. Brasquet: Polydysplasie avec hypoplasie dermique focale. *Ann Derm Syph* 33: 63 1966.
- Cole H. V. J. R. Druet H. K. Giffen C. B. Norris & G. Strud: Ectodermal and mesodermal dysplasia with osseous involvement. *Arch Derm Syph* 44: 773 1941.
- Cunha D. E. C. Pujasian & H. R. Selinger: Conrad's disease: Chondrodystrophia calcificans congenita: congenitally stippled epiphyses. *J Pediatr* 2: 63 1969.
- Daly J. F.: Focal Dermal Hypoplasia. *Cutis* 13: 4 1969. (Lit. Birth Defects Abstracts Sel. Artic. NF Mod 6: 84).
- Dumas P. P. Couderc P. Amblard & M. Callier: Une polydysplasie peu connue avec hypoplasie dermique en aires. *La Presse Méd* 16: 1189 1968.
- Freeman C. D. Jr.: Congenital ectodermal and mesodermal dysplasia. *Arch Derm* 71: 6 1955.
- Gilman M.: La polydysplasie avec hypoplasie dermique en aires. Thèse de Grenoble 1970 No 7.
- Gilman M., W. C. Peterson, R. J. Cronin & H. C. Ratcliffe: Ectodermal hypoplasia. *Arch Derm* 91: 69 1965.
- Gilman R. J., I. H. Meskinen, W. C. Peterson & R. W. Gilman: Focal dermal hypoplasia syndrome. *Acta Derm Vener* 43: 471 1963.
- Gilman R. J., I. H. Meskinen & W. C. Peterson: Congenital poikiloderma. *Brit J Derm* 65: 8 1968.
- Haley H. H. Haley & H. Clements: Poikiloderma congenitale. *Arch Derm Syph* 44: 34 1941.

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Summary

The 33rd case of focal dermal hypoplasia is reported The patient was a severely retarded blind and deaf woman aged 38 years She presented focal atrophies

pigmentations telangiectasies of the skin and fat herniations. The secondary sex characters were poorly developed. There was a monstrous dorsal kyphosis, lobster claw foot and other malformations of the hands and feet. The eyes were microphthalmic with bilateral colobomata of the irides and ectopia of both lenses. A survey of previously reported cases and a differential diagnostic discussion is given. Aetiological considerations are similar to those presented by incontinentia pigmenti, the orofacial digital syndrome, the Wilder-vanek syndrome and certain hereditary cases of congenital cataract and microphthalmia which all are restricted to females.

Key words: Focal dermal hypoplasia, microphthalmia, malformations of the eye, malformations of the skeleton, mental retardation.

References

- Baria L & J Lengyel: Über ein Syndrom mit naeviformen Hautatrophien (Systematisierte naeviforme Atrophodermie). *Ann. paediat.* 107: 208, 1966.
- Becker S W & D G Lindsay: A case for diagnosis: Thomson's poikiloderma. Ectodermal and mesodermal dysplasia with osseous involvement (Cole et al.). *Rothmund's syndrome?* *Arch. Derm.* 71: 670, 1958.
- Braun-Falco A & S Marghescu: Über eine systematisierte naeviforme Atrophodermie. *Arch. klin. & Exper. Derm.* 201: 249, 1963.
- Gallagher E J, M E MacGregor & M Israelshi: Chondrodystrophy with ectodermal defects. *Arch. Dis. Child.* 28: 14, 1953.
- Casala A, M C Bianchi, O Bianchi, J Mirande & R Brasquet: Polydysplasie avec hypoplasie dermique focale. *Ann. Derm. Syph.* 93: 63, 1966.
- Cole H V, J R Driver, H A Giffen, C B Norris & G Stroud: Ectodermal and mesodermal dysplasia with osseous involvement. *Arch. Derm. Syph.* 44: 773, 1941.
- Comings D E, C Papaian & H R Schoene: Conradi's disease: Chondrodystrophia calcificans congenita: congenital stippled epiphyses. *J. Pediatr.* 9: 63, 1963.
- Daly J F: Focal Dermal Hypoplasia. *Cutis* 4: 1334, 1963. (Lit. Birth Defects Abstracts, Ser. Artic. NF Mod. 69: 84).
- Dugois P, P Coude, P Amblard & M Gallier: Une polydysplasie peu connue avec hypoplasie dermique en aires. *La Presse Méd.* 76: 1189, 1968.
- Ferman C B Jr: Congenital ectodermal and mesodermal dysplasia. *Arch. Derm.* 71: 667, 1955.
- Gilien M: La polydysplasie avec hypoplasie dermique en aires. Thèse de Grenoble, 1967, No 7.
- Goltz R W, W C Peterson, R J Gorlin & H G Ravits: Focal dermal hypoplasia. *Arch. Derm.* 86: 93, 1962.
- Gorlin R J, L H Meskin, W C Peterson & R W Golt: Focal dermal hypoplasia syndrome. *Acta Derm. Vener.* 43: 471, 1963.
- Gold S: Poikiloderma congenitale (Thomson). *Brit. J. Derm.* 10: 318, 1938.
- Halsey H H, H Haily & H Clemens: Poikiloderma congenitale. *Arch. Derm. Syph.* 44: 345, 1941.

- Holden J D & W A Akers Goltz's syndrome Focal dermal hypoplasia Am J Dis Child 114 292 1967
- Holttinger A J Crottet A Franceschetti W Jadassohn & R Paillard Malformations multiples (incontinentia pigmenti atypica? polydactylie idiotie colobome de la cho roide) Dermatologica 122 50 1961
- Houell J B Naevus angiolipectimatosus vs Focal dermal hypoplasia Arch Derm 99 238 1965
- Jessner M Breslauer dermatologische Vereinigung Arch f Dermat u Syph 133 48 1921
- Jessner M Naeviforme poikilodermie artige Hautveränderungen mit Missbildungen (Schwimmbautbildungen an den Fingern Papillome am Anus) Zbl Hautkr 2/ 468 1928
- Jones J E & U S Seal X chromosome linked inheritance of elevated thyroxine binding globulin J Clin Endocr 27 1521 1967
- Liebermann S L Atrophoderma linearis maculosa et papillomatosis congenitalis Acta dermat venerol 16 476 1935
- Mannkopf H & F Hannev Zur Erscheinungsbild der kongenitalen ectodermalen Dys plasien V Graefes Arch Ophthalm 15 643 1957
- Martin Scott I Congenital focal dermal hypoplasia Brit J Derm 77 60 1965
- McKusick V A Heritable disorders of connective tissue 3rd edit C V Mosby 1966
- Miedinski F Naevus lipomatodes superficialis Dermatologica 126 223 1963
- Naegeli O Poikilodermie Zbl Hautkr 23 638 1927
- Nickel W R & J H Lockwood Congenital ectodermal dysplasia with associated mesodermal defects Arch Derm 74 327 1956
- Patau K E Therman S L Inhorn D W Smith & A L Russ Partial trisomy syn dromes II An insertion as cause of the OFD syndrome in mother and daughter Chromosoma 12 578 1961
- Rook A Poikiloderma congenitale Rothmund Thomson syndrome Acta Dermat vener 39 392 1959
- Salamon T Z Jevtic & O Laovic Über eine eigenartige Form der Aplasia (Hypo plasia Cutis congenita mit multiplen hypoplastischen Fehlbildungen) Arch klin u exper Dermat 217 295 1963
- Shotts N & A E H Emery Bloch Sulzberger syndrome (Incontinentia pigmenti) J Med Genet 3 148 1966
- Waardenburg P J in Waardenburg Franceschetti & Klein Genetics and Ophthal mology Royal VanGorcum Netherland 1961 page 355
- Wahrman J M Berant J Jacobs I Aviad & N Ben Hur The oral facial digital syndrome A male lethal condition in a boy with 47 XXY chromosomes Pediatrics 37 812 1966
- Walbaum R G Samaille & Ph Dehaene Syndrome de Goltz chez un garçon Com munication presentee a la Soc de Pediatrie de l'Est et du Nord (Filiale de LILLE) le 8 Novembre 1969
- Walter F Hypoplasia cutis cong Arch Derm 90 340 1964
- Wilson H T H Congenital telangiectasia with dysostosis Proc 10th internat Congr Derm (London) 1952 p 510
- Wodnianski P Über die Formen der kongenitalen Poikilodermie Arch f klin u exper Dermat 205 331 1957
- Golt R W R R Henderson J M Hutch & J E Ott Focal dermal hypoplasia syndrome Arch Derm 101 1 1970

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COLOURED GLASSES AND COLOUR VISION WITH REFERENCE TO CAR DRIVING

BY

LENNART BERGGREN

In Sweden there is no legal ban whatsoever against car drivers wearing coloured glasses. On the other hand it is not permitted for subjects with colour defects of any kind to drive buses (4, 7). These facts would clearly be in conflict with each other if there were a conceivable risk that coloured glasses might cause faulty colour reproduction.

In the present investigation we have tried to analyze the question of the effect on colour vision by coloured glasses. Normal subjects were tested on their ability to do an anomaloscopic colour match with different kinds of coloured glasses. Their ability to interpret pseudoisochromatic plates was also investigated.

It is generally believed and implied that coloured glasses (sun glasses) of good quality reproduce natural colours, i.e. that visible radiation is transmitted as evenly as possible. Ultraviolet and infrared rays should be absorbed as much as possible. It was surprising and unexpected to find out that coloured glasses even from well known manufacturers were not regularly sold with a transmission spectrum or a relevant description of the characteristics of the glasses in question. The glasses were claimed to reproduce natural colours and an information of an average percentage figure of absorption was also given. Such a figure suggests an even transmission and is misleading if that is not the case. Apparently there seems to be little demand for exact information of transmission properties and the perfection of the glasses is taken for granted.

Use of coloured glasses The main purpose of coloured glasses is to prevent

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strong light from reaching the eye. The medical use of coloured glasses is limited chiefly to conditions causing photophobia such as allergic conjunctivitis, iritis, opacities in the lens and vitreous body and so on.

Much of our visual information is based on our capacity to discriminate between differences of brightness. The differential sensitivity is constant only in luminosities in the middle range and considerable deviations occur in high and low intensities. In sunshine the power of discrimination becomes diminished and visual acuity decreases. Absorptive glasses used in bright sunshine extend the range of constant differential sensitivity.

Another advantage of coloured glasses may be worth mentioning. Prolonged stay in strong sunlight decreases the dark adaptation process (5). The intensive bleaching of visual purple over a long period of time results in a utilization of released vitamin A in other parts of the body. When twilight sets in the vitamin A supply is insufficient and the dark adaptation process will be more sluggish.

Coloured glasses are widely used as a protection from glare. Glare is caused by the scatter of light from imperfections in the optical media, mainly opacities in the lens and the vitreous. The stray rays veil the vision and very bright light causes a temporary scotoma. The sensation of glare increases with age due to increasing opacities in the optical media (11).

Misuse of coloured glasses. Commercial advertising has exploited colour appearance, concealing effects and other unessential qualities of sunglasses. This has unquestionably led to a misuse among certain groups of the population.

The conception that the absorption by coloured glasses could do harm to the eye is however not justified. Normal illumination changes during the day without glasses are obviously much greater than sunglasses of 15-90 per cent absorption could ever achieve. In other words, contrast discrimination can be diminished and in very low illumination also the visual acuity by the use of coloured glasses. Permanent harmful effects to the eye, however, are unknown (10).

Material and Methods

The test subjects comprised ten normal females with an age of 20-30 years.

The following different coloured glasses were tested:

POL Polaroid 65 per cent absorption, grey colour (Polaroid Co USA)

RBG Ray Ban G 31 69 per cent absorption, grey colour (Bausch and Lomb USA)

RB 3 Ray Ban Shade 3 69 per cent absorption, green colour (Bausch and Lomb USA)

RL 50 Rosa Lux 50 per cent absorption brown colour (Uppsala Optiska Industri Sweden)

RL 70 Rosa Lux 70 per cent absorption brown colour (Uppsala Optiska Industri Sweden)

U 65 Umbral 65 per cent absorption brown colour (Carl Zeiss Germany)

U 85 Umbral 85 per cent absorption brown colour (Carl Zeiss Germany)

UP 65 Umbra Punktal 65 per cent absorption brown colour (Carl Zeiss Germany)

UP 85 Umbra Punktal 85 per cent absorption brown colour (Carl Zeiss Germany)

UG Undefined glasses These glasses were sold in a car service station as sunglasses fit for drivers No quality declaration was given

Transmissive properties in the visible spectral range 400 700 nm of the nine kinds of glasses from the stated manufacturerers are given in fig 1

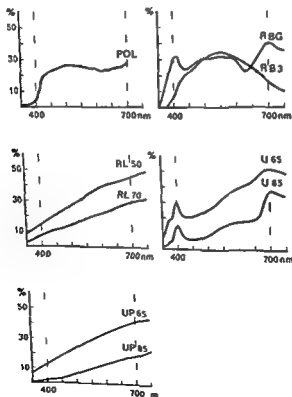


Fig 1
Transmission spectra in the visible region 400 700 nm of nine different coloured glasses

Anomaloscopic examination The modern model of the Nagel anomaloscope was used (Schmidt and Haensch Germany) The normal value of the experimental apparatus was 41/16 for the green red/yellow adjustment = a green red quotient of 1.0

Each subject established her own colour match without glasses and with each of the ten test glasses The colour matches were done in a variable order and with five trials for each colour match

The pseudoisochromatic plates by Boström Kugelberg (B K) and Bostrom (II B) are used in the official pseudoisochromatic colour vision test in Sweden There are 20 B K plates and 16 II B plates The subjects were tested without glasses and with the different glasses The method and the subjective and objective evaluation will be further described under Results

Results

The mean results and ranges of the anomaloscope examination expressed in absolute apparatus figures and green red quotients are given in table I and fig. 2 It is immediately seen that only Polaroid glasses (POL) and Ray Ban G 31 glasses (RBG) fit a normal Rayleigh equation The mean green red quotient from one of the other glasses was at the protanomalous border and the remaining seven glasses gave "deuteroanomalous" green red quotients Glasses with high absorptive properties more markedly affected the colour match

The obvious reasons for these results are the different transmissive properties of the glasses as shown in fig. 1 The absorption is not even in the visible part of the spectrum Brown glasses cut off more of the short wave lengths and green glasses cut off short and long wave lengths Only grey glasses show an even absorption It is thus clearly misleading when an average absorption figure is used in order to describe the quality of glasses An example of this is given in fig. 3 showing three glasses of similar average absorption but with very different transmission spectra

It should also be pointed out that the general subjective opinion of the test subjects was that the different glasses when used under normal conditions reproduced natural colours The faulty colour reproduction was only revealed by the anomaloscope It has thus been shown that the qualitative as well as quantitative absorption of coloured glasses is of importance in the anomaloscopic colour matches It is also evident that the adjustment variability was greater when glasses with high absorptive properties were used

The ability to interpret pseudoisochromatic plates turned out to be difficult to evaluate in an objective manner If the subjects were allowed enough time they often passed the test also with glasses The test was therefore run without

Table I

Anomaloscopic determinations without and with ten different coloured glasses. Ten female subjects. Mean apparatus figures and green red quotients are given as well as individual mean ranges and individual adjustment ranges.

Type of coloured glasses	Scale readings			Green red quotient	
	Group mean	Range	Individual adjustment Range	Group mean	Range
No glasses	39.8	38.2-41.0	0 - 3.0	1.07	1.15-0.99
POL	39.7	38.2-41.5	0.5- 6.0	1.01	1.15-0.97
RBG	39.5	37.4-42.3	1.0- 6.5	1.08	1.22-0.92
RB 3	47.3	45.7-49.3	1.5- 8.0	0.68	0.67-0.76
RL 50	35.7	33.3-38.7	0.5- 7.0	1.35	1.50-1.15
RL 70	33.8	31.9-35.9	1.0-10.0	1.50	1.65-1.30
U 65	34.6	32.9-36.5	1.0-10.5	1.43	1.55-1.77
U 85	30.9	29.4-33.8	0.5- 8.5	1.74	1.90-1.50
UP 65	35.4	33.7-38.1	1.0- 5.5	1.35	1.50-1.17
UP 85	31.1	27.3-34.5	2.5- 6.0	1.71	1.93-1.42
UG	24.4	22.5-26.6	1.5- 5.0	2.53	2.83-2.40

glasses in the shortest possible time with no errors allowed. The test was then repeated with the different glasses noting time and errors (see table II). During these experiments two things became evident. First the experiment had to be done binocularly. In monocular speed experiments the test subjects complained of fatigue and blurring and often failed on several plates also without any glasses. Secondly the 36 plates became in the long run too familiar to the subjects and a figure could be interpreted without exactly recognizing it. A cautious interpretation is that high absorptive coloured glasses seemed to decrease speed and increase the number of errors. It was not possible to separate adequately between the different glasses with this method.

A subjective judgment of separation between the different glasses in the pseudoisochromatic test is accounted for in table II. The subjects were asked to value the test without and with the ten different glasses in figures from 1 to 11 in order of increasing difficulty. Thus figure 11 signifies the most difficult test and the figure 1 the easiest test. The subjective impression agrees astonishingly well with the degrees of difference of the green red quotients from the normal value established in the anomaloscopic examination. The test

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Table II

Judgment of 36 pseudoisochromatic plates without and with different coloured glasses
 Objective estimation by interpretation time in seconds and number of wrong answers
 Subjective estimation of test by figures in order of increasing difficulty

	Objective estimation Interpretation time in secs		Number of errors		Subjective estimation (1-11) 1 = easiest test 11 = most difficult test	
	M	Range	M	Range	M	Range
No glasses	61	34-117	0	-	10	-
POI	74	43-132	10	0-2	3.6	2-9
RBG	67	44-100	13	0-3	4.9	3-8
RD 3	61	42-123	17	0-4	6.6	2-10
RL 50	63	32-136	0.6	0-2	4.3	2-7
RL 0	62	39-102	1.2	0-3	6.1	4-8
U 63	57	38-108	1.0	0-3	4.7	2-7
U 83	77	50-147	1.7	0-5	8.5	5-11
UP 63	63	44-142	1.1	0-5	6.1	2-9
UP 83	80	49-127	2.4	0-8	9.8	9-11
LG	10	42-91	2.6	0-7	10.7	10-11

subjects did not know the outcome of the anomaloscopic examination when asked to make the subjective judgment

Discussion

The subjective impression that coloured glasses in general are accepted as reproducing natural colours is probably due to the capacity of colour adaptability (10). Colour matches in the anomaloscope reveal the transmissive properties of such glasses and their possible faulty colour reproduction. Green red quotients outside the normal range and an increased range of variation in adjustment are similar to the colour matches done by colour defectives of the deuteranomalous and protanomalous type.

In Sweden as well as in several other countries colour defective bus drivers are not permitted. To the writer's knowledge there is nowhere any restriction against the use of coloured glasses of any kind of quality for car or bus drivers. The inconsistency is obvious from the present results. Only permission to

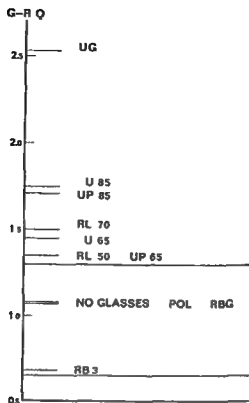


Fig 2

Mean anomaloscopic colour matches by ten female subjects without and with coloured glasses Normal green red quotient = 1.0 Normal range 0.65-1.3

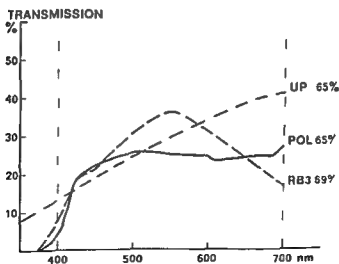


Fig 3

Comparison of transmission spectra of three different glasses with about similar absorption POL 65% RB 3 69% and UP 65 65%

References

- 1 Committee on Medical Aspects of Automotive Safety Visual factors in automobile driving and provisional standards Arch Ophthal 81 863 1969
- 2 Gramberg Danielsen B Untersuchungen über die Unfallhäufigkeit von Farbenuntüchtigen im Strassenverkehr Klin Mbl Augenheilk. 139 617 1961
- 3 Gramberg Danielsen B Farbenuntüchtigkeit und Strassenverkehr Zentralbl Verlehrs Med 11 1 196
- 4 Granstrom K O Synkrav för korkort specialfall och gransfall Lakartidn 63 346 1968
- 5 Hecht S., Hendley C D Ross S & Richmond P A., The effect of exposure to sunlight on night vision. Am. J Ophthal 31 1575 1948
- 6 Hugelberg I 1 Betänkande med förslag till åtgärder för höjande av trafiksäkerheten. SOU 90 1948
- 7 Medicinalstyrelsens cirkular MF 99 1963
- 8 Norman L G Medical aspects of road safety Lancet 1 1039 1960
- 9 Shirley S Y & Gauthier R J Recognition of coloured lights by colour defective individuals Canad J Ophthal 3 244 1968
- 10 Schober H Fur und wider Sonnenbrille Deutsche Med Wschr 86 1249 1961
- 11 Wolf E Glare and age Arch Ophthal 64 507 1960
- 12 WHO Symposium 1967 Human factors in road accidents WHO Copenhagen 1968

drive for colour defectives (at least of the anomalous type) or a ban against driving with undefined coloured glasses would make sense

Two circumstances can be pointed out which question the validity of the importance of normal colour vision in traffic. A great many drivers undoubtedly wear coloured glasses at least in the summertime. However, it has not been revealed that the colour of the glasses has played any significant role in violations against traffic laws. Nor have controlled large scale studies on colour defective and colour normal drivers been able to show any difference in accident frequency (2, 3, 8). In fairness to an opposite opinion it can be noted that although the WHO recommendations in 1956 discounted colour discrimination as a factor in safe driving, the question was apparently not settled since there was a sharp division of opinion on the issue in the WHO Symposium 1967 (12). It was concluded by the participants that more information was needed. In the latest recommendations in 1969 of the Committee on medical aspects of automotive safety in U.S.A. (1) colour vision is not considered important. It is only required that the applicant must distinguish the basic traffic control colours of red, green and amber. Under artificial conditions (colour vision tests) where colour is the only clue, colour defectives make much more mistakes than in actual driving (9).

The controversy in opinions about colour defective car drivers is unnecessary. It is the signal system that could and should be made safe for everybody including colour defectives and carriers of coloured glasses. It is disappointing that proposals of the use of symbol lights (bars, squares, diamonds etc.) (2, 6, 9) have not been carried out. The use of symbols and hues as remote as possible on the spectrum in street lights, flashing signals and rear red lights would lead to much less confusion. Such a system would be of great value for safe driving also by colour normal subjects.

Summary

Female subjects with normal colour vision 20-50 years of age were tested on their ability to do an anomaloscopic colour match and to interpret pseudoisochromatic plates without and with coloured glasses (sun glasses) of ten different kinds. It was found that even glasses of supposed good quality markedly affected colour matching to green-red quotients outside the normal range. Only with two kinds of glasses, the Polaroid glasses and the Ray-Ban G-31 glasses, was it possible to do a normal colour match. The interpretation of pseudoisochromatic plates was impaired by glasses with high absorptive properties. The findings are discussed mainly in relation to the question of whether colour discrimination plays any role in safe driving.

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ROSE BENGAL VITAL STAINING

Staining of Cornea and Conjunctiva
by 10 % Rose Bengal Compared with 1 %

BY

M S NORN

The first time rose bengal was used in the eye region seems to have been in 1914 (Romer Gebb & Löhlein). The dye was used together with safranin and Victoria yellow to combat pneumococcal infection (quoted by Marx 1924).

Kleefeld (1919) was the first to use rose bengal as a vital stain for staining corneal ulcer (quoted by Marx 1924).

Marx in 1924 and 1926 subjected rose bengal vital staining to a careful study especially the punctate staining seen on the conjunctiva along the ciliary margin. (This line I have found it proper to name Marx line (Norn 1966)).

Sjogren uses 1 % rose bengal for diagnosing keratoconjunctivitis sicca. The classical M D thesis is from 1933.

In normal eyes Sjogren occasionally finds staining along the ciliary margin on the caruncle, the central portion of the semilunar fold and possibly in a minor proportion on the bulbar conjunctiva nasal to the cornea.

In various studies (Norn 1962, 1964 A, 1969 B) I arrived at the result that rose bengal stains degenerate cells. The cell nucleus assumes an intenser red colour than the cytoplasm. Cells are stained at different intensities, slightly degenerate cells assuming a weaker colour than highly degenerate cells. Dead cells get an intense red colour.

Mucus is likewise stained by rose bengal. Double staining with rose bengal and the mucus specific alcian blue gives a specific colouring: degenerate cells become red (rose bengal) and mucus blue (alcian blue).

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tensely in all the regions studied cornea, bulbar conjunctiva semilunar fold caruncle inferior fornix inferior tarsus and conjunctiva along the ciliary margin termed Marx line.

The total material is found recorded in table 2 (the percentage number of eyes stained) and in fig 1 (mean colour intensity in region concerned)

Note that the colour intensities differed appreciably e. g. from 0.6 to 1.4 from 1.14 to 2.65 and from 2.35 to 3.25 in other words often a rise of one grade by using 10% instead of 1% rose bengal

The higher dye concentration also greatly raised the number of corneae stained Thus for instance only 53 per cent of the corneae were stained by 1% rose bengal against 19 per cent by 10% rose bengal The inferior fornix was stained in 4 and 16 per cent respectively

The stainability of the cells depends in other words definitely on the dye concentration

Normal Eyes

In general a vital stained region of the conjunctiva or cornea is reckoned as a sign of a pathological process However conjunctival regions are found which usually become stained even in normal eyes The staining is more frequent and more pronounced using 10% rose bengal compared with 1% rose bengal

The frequency of staining and the mean colour intensity are recorded in table 3 for the 43 normal eyes after staining with 10% rose bengal The colour was weaker on the cornea, bulbar conjunctiva inferior tarsus and Marx line than in the pathological cases

The cornea is only weakly stained by rose bengal 1% In the present series 40 per cent were stained generally of the lowest grade The intensity averaged grade 0.60 in the whole normal series (0.79 in the total series)

Staining was found to be most frequent among the elderly subjects A mean grade above 1 was seen in the subjects over 60 years of age

The slight staining of the cornea of normal eyes by 1% rose bengal had the form of few red dots close to the limbus nasally (8 cases) below and nasally (6 cases) or elsewhere (3 cases)

The 10% rose bengal concentration gave staining in as many as 77 per cent and a mean colour intensity of grade 1.7 The number of normal eyes stained rose with increasing age. The great majority of the subjects over 40 showed staining (30 out of 32)

The mean colour intensity was likewise higher the older the subjects Grouping in 10 year age classes gave mean grades of 0.2 1.3 1.6 1.8 2.3 and 3.0 for the 10 20 30 40 50 60 and 70 + 80 year age groups respectively

rose bengal was instilled likewise from a needle mounted tube. The drop was placed on the bulbar conjunctiva above and lateral to the cornea while the subject was looking down and nasally.

Preliminary investigations have shown that the high rose bengal concentration may cause staining at the site of application, where the undiluted dye drop gets in direct contact with the epithelium before blinking and before the tear flow distributes it evenly in conjunctival fluid and precorneal film.

I therefore preferred to apply the 10 % dye solution to an area which usually remains unstained.

Unlike this solution 1 % rose bengal seems not to cause extra staining at the site of application.

Vital staining after instillation of 10 % rose bengal was studied in the slit lamp graduated and the results were entered in a diagram.

Material

A total of 100 eyes of 89 subjects were examined. 43 eyes were normal and 57 pathological. The diagnoses are shown in table 1.

Results

Comparison of vital staining with 10 % and 1 % rose bengal respectively gave the result that the higher concentration stained more frequently and more in

Table 1
Clinical diagnoses of 100 eyes subjected to vital staining by 1 % and by 10 % rose bengal

normal eyes	43
erosion foreign body in cornea corrosion	6
dendritic keratitis	6
other keratitis	10
keratoconj sicca	4
contact lens wearer	3
infectious conj	7
chronic simple conj	7
lagophthalmos ectropion	11
others	8

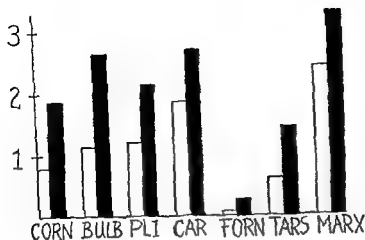


Fig 1

Mean colour intensity on the cornea and different parts of the conjunctiva after vital staining by 1% bengal (white columns) and 10% rose bengal (black columns). A total of 100 eyes examined. Arbitrary grading (ordinate).

Table 3

Mean grades of colour intensity at different sites after vital staining with 10% rose bengal in the normal series (43 eyes) and the total series (100 eyes)

	cornea	bulb conj	fold	caruncle	inf fornix	inf tarsus	Marx line
normal eyes	1.7	2.3	2.2	2.6	0.4	1.3	3.0
total series	1.59	2.63	2.12	2.66	0.26	1.40	3.21

The staining of the cornea in normal eyes by 10% rose bengal likewise often consisted of rather few red dots localized close to the limbus nasally (4 cases) below and nasally (14 cases) or inferiorly (4 cases). In two slight staining was seen elsewhere.

In five cases scattered dots were seen all over. The remaining four cases were interesting in that the staining after instillation of 10% rose bengal corresponded exactly to that which may be found in patients with keratoconjunctivitis sicca after instillation of the usually employed 1% rose bengal (see later).

Table 2
Percentage numbers of eyes stained by the vital stain concerned at the sites concerned

	cornea	bulb conj	fold	caruncle	inf fornix	inf tarsus	Marx line	Number of eyes
rose bengal 1%	53	64	66	90	4	85	99	100
rose bengal 10%	79	93	90	99	16	62	100	100
methylene blue	47	70	76	95	33	81	57	100
trypan blue	40	60	70	95	9	48	74	100
bromothymol blue	8	8	8	42	11	23	23	156

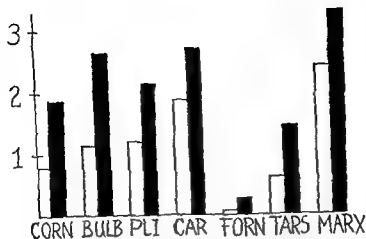


Fig 1

Mean colour intensity on the cornea and different parts of the conjunctiva after vital staining by 1% bengal (white columns) and 10% rose bengal (black columns) A total of 100 eyes examined Arbitrary grading (ordinate)

Table 3

Mean grades of colour intensity at different sites after vital staining with 10% rose bengal in the normal series (43 eyes) and the total series (100 eyes)

	cornea	bulb conj	fold	caruncle	inf fornix	inf tarsus	Marx line
normal eyes	1.7	0.3	2.2	2.6	0.4	1.3	3.0
total series	1.89	0.63	2.12	2.66	0.56	1.40	3.21

The staining of the cornea in normal eyes by 10% rose bengal likewise often consisted of rather few red dots localized close to the limbus nasally (4 cases) below and nasally (14 cases) or inferiorly (4 cases) In two slight staining was seen elsewhere

In five cases scattered dots were seen all over The remaining four cases were interesting in that the staining after instillation of 10% rose bengal corresponded exactly to that which may be found in patients with keratoconjunctivitis sicca after instillation of the usually employed 1% rose bengal (see later)

The *bulbar conjunctiva* is stained more frequently and more intensely than the cornea 1% rose bengal gave staining in 67 per cent mean grade 1.0 The colour intensity rose perhaps a little with increasing age but apparently not the frequency The sites were most often close to the limbus nasal to the cornea (14 cases) below and nasally (12 cases) or inferiorly (3 cases) Diffuse sicca-like staining was not observed in normals after 1%

After instillation of 10% rose bengal staining was more frequent (98 per cent) and more intense (mean grade 2.3) The colour intensity did not rise significantly with increasing age (calculated for 10 year age groups the mean grades were 1.3 1.6 2.7-2.1 2.8 1.9 2.9)

Punctate staining was most frequently seen close to the corneal limbus nasally (6 cases) below and nasally (21 cases) or inferiorly (8 cases)

Using 1% rose bengal staining was most frequent nasally After instillation of 10% the dye most often spread downwards below and nasally thus being the most frequent site

In three cases the 10% rose bengal gave staining temporally close to the site of application In the remaining four cases sicca like staining was seen

The latter four subjects were all women over 50 with no symptoms

After instillation of the usually employed 1% rose bengal the cornea remained unstained, while the bulbar conjunctiva showed few red dots nasal to the limbus corneae

10% rose bengal on the other hand gave pronounced punctate staining on the exposed part of the cornea extending to the exposed part of the bulbar conjunctiva in exactly the same manner as seen after instillation of 1% rose bengal into eyes with typical keratoconjunctivitis sicca

It is tempting to regard these normal cases as asymptomatic precursors of keratoconjunctivitis sicca

The *semilunar fold* and the *caruncle* were stained in many cases by 10% rose bengal (fold 39 out of 43 caruncle all) The colour intensity and frequency were independent of age and did not differ significantly from the corresponding values in the pathological series

The *inferior conjunctival fornix* was rarely stained (9 out of 43 cases) The staining was independent of age and did not differ from that in the pathological cases

The *inferior tarsus* was stained by 10% rose bengal in 28 out of 43 cases The colour intensity was not age determined but was less pronounced than in the pathological cases

Marx line was in all cases stained by 1% rose bengal and more intensely so by the 10% concentration The colour intensity was perhaps a little lower in the age group under 30 (after 10% rose bengal the mean grades within 10 year age groups were 1.3 2.0 3.7 3.3 3.5 3.0 3.1) The colour intensity was higher in the pathological cases

Sex Difference

The mean colour intensity was higher in females than in males

The mean grades calculated for all sites were 2.15 for females and 1.71 for males after 10% rose bengal and 1.11 and 0.91 respectively after 1% rose bengal

Such a difference was seen even after correction for age variation in the normal series

The sex difference was pronounced for the inferior fornix and the inferior tarsus significant for the caruncle and the semilunar fold and less significant for Marx line while the cornea showed no sex difference

The sex difference seemed to exist within all age classes both after 1% and after 10% rose bengal

Pathological Eyes

Corneal Diseases

Corneal defects were stained more intensely by 10% rose bengal compared with 1%

In a case of *dendritic keratitis* only few and uncharacteristic elements were visible after instillation of 1% rose bengal whereas after 10% several characteristic dendritic elements were seen

One eye affected with chronic *adenovirus keratitis* was stained neither by fluorescein nor by 1% rose bengal. The 10% rose bengal concentration gave uniformly stained elements scattered over the whole cornea

In a case of punctate superficial keratitis (of *Thygeson's* type) 1% rose bengal left only few scattered uncharacteristic red elements whereas 10% rose bengal gave characteristic staining of keratitis elements

One eye with *marginal keratitis* and one with *Aster ophthalmicus* were stained by 10% rose bengal but not by 1%

Corrosions of the cornea and conjunctiva were stained more intensely by 10% rose bengal than by 1% and the corroded areas were more sharply demarcated from the normal cornea and conjunctiva (Accidents with ammonia, hydrochloric acid, nitric acid or slaked lime). In one case corrosion was not recognizable after 1% rose bengal but the region became intensely stained by 10% rose bengal

Corneal oedema displayed diffuse punctate staining after instillation of both 1% and 10% rose bengal. The staining was most intense after the latter

A corneal graft remained unstained after both 1% and 10% rose bengal. Use of the latter is supposed to constitute a more sensitive test for the vitality of the graft than 1% rose bengal

Contact lens wearers were found to have their cornea, bulbar conjunctiva,

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Staining at the Site of Application

The region touched primarily by the 10% rose bengal drop was exposed to a massive dye concentration until subsequent blinking spread the dye over the entire conjunctival sac and the precorneal film

The intense staining by the 10% concentration may manifest itself as a local artificial colouring unlike the true vital staining which depends on the degeneration of the epithelial cells and which is seen at a greater distance from the site of contact

In eight cases 10% rose bengal was instilled laterally in the inferior fornix and in four in the outer canthus. In seven of the above 12 cases this instillation may have raised the colour intensity recorded in the region concerned

In the remaining 88 cases 10% rose bengal was instilled above and temporally on the bulbar conjunctiva while the subject was looking down and nasally. The drop thereby fell on a region which usually is not vital stained

Local staining at the site of application was observed in 63 of the 88 cases often of a weak intensity (grade 1 in 22 grade 2 in 24 grade 3 in 13 grade 4 in 4 and grade 5 in 2 cases) independent of the clinical diagnosis

The stained area was small 1-4 mm in diameter circular or prolonged downwards

In some instances the lower limit was linear horizontal because the concentrated dye drop was stopped in its gravitational flow downwards by the lower ciliary margin.

No similar phenomenon was noticed after instillation of the weaker 1% rose bengal

Mucus

Rose bengal stains both degenerate cells and mucus. Vital staining with 1% alcian blue after rose bengal shows which of the originally red spots represent mucus and which degenerate cells the former now becoming blue while the latter remain red

After staining first with 1% rose bengal the normal cornea for instance may show that about half of the originally red dots are mucus and the remainder degenerate epithelial cells (Norn 1964 A)

Instillation of 10% rose bengal gave a more intense colour. Subsequent vital staining by alcian blue only disclosed the usually fairly small amount of mucus

The increased vital staining by 10% rose bengal was due to the fact that a greater number of mildly degenerate cells became vital stained while the mucus now constituted a minor proportion only of the vital stained regions

tarsus and Marx line of upper and lower lid more intensely stained by 10% than by 1% rose bengal. Rose bengal staining shows where the contact lens exerts a pressure being thus useful as an aid to deciding where the lens may need some modification.

Keratoconjunctivitis Sicca

In cases with established keratoconjunctivitis sicca even 1% rose bengal gave characteristic staining in the form of a band across the exposed part of the cornea. The band extended further across the exposed part of the bulbar conjunctiva (fig 2).

The colour became more intense with 10% rose bengal and in some instances extended further also below the cornea.

In mild cases of keratoconjunctivitis sicca 1% rose bengal gave a weaker colour, whereas 10% rose bengal stained intensely and characteristically.

Conjunctival Diseases

The cases of infectious conjunctivitis did not differ significantly from the normal series except that in a small number of cases 10% rose bengal gave more intense staining inferiorly on the bulbar conjunctiva.

Eyes with *chronic simple conjunctivitis* did not differ from the normal eyes.

In *ectropion* and *lagophthalmos* better staining of the exposed conjunctiva was obtained with the higher rose bengal concentration. Likewise corneal damage was more easily detected with this concentration in *trichiasis* and *entropion*.

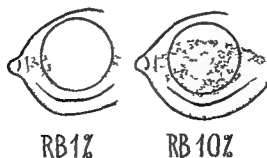


Fig 2

A mild case of keratoconjunctivitis sicca vital stained by 1% rose bengal (left figure) and the same eye after vital staining by 10% rose bengal (right figure).

The degrees of solubility of the other vital stains mentioned above are such that use of higher concentrations hardly is permissible.

As a general rule we may say that 10% rose bengal stains more frequently and more intensely in all the regions than the other vital stains studied

An exception from this rule is constituted by 1% methylene blue which stains more frequently and more intensely in the inferior fornix and the inferior tarsus

This more intense staining is however presumably false methylene blue tending to precipitate as granules which are caught by mucus and therefore occur particularly in regions rich in mucus within the inferior fornix and tarsus where the dye drop has been instilled

The main conclusion to be drawn must therefore be that 10% rose bengal is the best vital stain for detection of degenerate epithelial cells

A scale of increasing cell degeneration and cell death can be set up The sound cell is not stained by rose bengal The mildly degenerate cell is stained by 10% rose bengal only and the more degenerate cell also by 1% rose bengal while the dead cell is stained by 1% rose bengal and also by 1% trypan blue (Norn 1969 B)

Rose bengal may disclose degenerate epithelial cells on the cornea and bulbar conjunctiva even in normal eyes This phenomenon increases in frequency and intensity in the higher age classes and is more frequent in the conjunctiva of females than in that of males

The female preponderance of degenerate epithelial cells is possibly due to special properties of the conjunctival fluid and the precorneal film In a previous study I found the precorneal film to be less stable in women than in men (Norn 1969 A)

In normal eyes rose bengal stains particularly nasal and lower regions at the limbus corneae

By vital staining with fluorescein micropunctate colouring of the cornea has been shown in 17 per cent of normals (Norn 1970) The colouring was seen to rise in intensity with increasing age and to be located in the same region of the cornea.

We may thus conclude that the region extending nasally below and nasally and inferiorly round the limbus corneae is particularly vulnerable this region being in normals liable to epithelial cell degeneration of the cornea and conjunctiva and microlesions of the cornea

The phenomenon is not identical with the cold injury phenomenon described by Holstad in skiers The latter is one of rose bengal staining of the lower part of the cornea and bulbar conjunctiva a region bounded above by an upwards convex line Holstad's phenomenon is perhaps due to freezing of tears accumulated in the middle of the inferior fornix.

The phenomenon described in this paper may possibly be due to physiologi

Side-Effects

In some cases 1 % rose bengal may cause smarting, while in others the instillation has no such disagreeable effect. It is my impression that rose bengal smarts particularly in the eyes where extensive vital staining is seen e.g. in keratoconjunctivitis sicca.

Rose bengal may precipitate, even in a 1 % aqueous solution. These dye grains may cause mechanical irritation.

The rose bengal used is from the British Drug House. No preservatives nor substances for the sake of isotonia have been added because the dye itself has a certain unknown osmotic effect.

In some cases I used 10 % rose bengal without previous local anaesthesia. Some of these subjects felt a pronounced smarting pain, while a small number felt no pain.

Previous novesin anaesthesia seems to cause no artificial vital staining. No more does it alter the wetting properties of the precorneal film (Norn 1969 A).

Compared with the usually employed 1 % rose bengal, the 10 % concentration naturally has the disadvantage that it may give undesired colouring of eyelids, cheek, fingers and clothes. To avoid this I used the needle mounted tube with its smaller drop size. The needle may however tend to become clogged from one day to the next owing to precipitations of the concentrated dye solution in the lumen.

Vital staining even by 10 % rose bengal declines at a fairly fast rate. After 20-30 minutes most of the stained regions have grown pale or lost all colour.

Permanent colouring (tattooing) has never been observed after rose bengal.

Discussion

The present study comprised a direct comparison of staining with 1 % and with 10 % rose bengal in different regions.

In a similar manner I have previously compared 1 % rose bengal with 1 % methylene blue, with 1 % trypan blue and with 0.2 % bromothylene blue (Norn 1967 A, B 1968).

1 % rose bengal thus constituted the basis of a comparison with the stated vital stains.

The materials investigated were not identical however. For instance the present series included a greater number of normal subjects than the others. Nevertheless the mean colour intensity with 1 % rose bengal was approximately the same in the four series. A comparison is therefore judged to be justified.

The semilunar fold, caruncle and conjunctiva along the ciliary margin (Marx line) were seen to become stained in nearly all the normal eyes

Use of 10% rose bengal is to be recommended in pathological states where 1% fluorescein and 1% rose bengal have given no vital staining

In the series under review instillation of 11% rose bengal disclosed cases of dendritic keratitis, punctate keratitis, corrosion and keratoconjunctivitis sicca

Familiarity with stainability in normal eyes is required to be able to interpret the colouring observed especially after instillation of 10% rose bengal

References

- Hoult David A & Joseph H Golstein: Physiologic lagophthalmos. *Am J Ophthalm.* 68 333-336 (1969)
- Kolstad Albert & Røald Opsahl jr: Cold injury to corneal epithelium. *Acta Ophthalm.* 47 656-659 (1969)
- Marx E: Über vitale Färbungen am Auge und an den Lidern. I. *Graefes Archiv f. Ophthalmologie* 114 463-482 (1974)
- Marx E: Über vitale Färbung des Auges und der Augenlider II. *Graefes Archiv f. Ophthalmologie* 116 114-125 (1976)
- Norn M S: Vital staining of cornea and conjunctiva. *Acta Ophthalm.* 40 389-401 (1967)
- Norn M S: Specific double vital staining of the cornea and conjunctiva with rose bengal and alcian blue. *Acta Ophthalm.* 42 84-96 (1964 A)
- Norn M S: Fluorescein vital staining of cornea and conjunctiva. *Acta Ophthalm.* 42 1033-1043 (1964 B)
- Norn M S: Vital staining in practice using a mixed stain and alcian blue. *Acta Ophthalm.* 42 1046-1053 (1964 C)
- Norn M S: Lacrimal apparatus tests: a new method (Lacrimal streak dilution test) compared with previous methods. *Acta Ophthalm.* 43 557-563 (1965)
- Norn M S: Vital staining of canaliculus lacrimalis and the palpebral border (Marx line). *Acta Ophthalm.* 44 948-959 (1966)
- Norn M S: Methylene blue (Methylthionine) vital staining of cornea and conjunctiva. *Acta Ophthalm.* 45 347-358 (1967 A)
- Norn M S: Trypanblue vital staining of cornea and conjunctiva. *Acta Ophthalm.* 45 350-359 (1967 B)
- Norn M S: Bromo thymol blue. *Acta Ophthalm.* 46 231-242 (1968)
- Norn M S: Desiccation of the precorneal film I. Corneal wetting time. *Acta Ophthalm.* 47 86-88 (1969 A)
- Norn M S: Dead, degenerated and living cells in conjunctival fluid and mucous thread. *Acta Ophthalm.* 47 1102-1115 (1969 B)
- Norn M S: M. punctate fluorescein staining of the cornea. *Acta Ophthalm.* 48 103-118 (1970)
- Sjogren H: Zur Kenntnis der Keratoconjunctivitis sicca. *Acta Ophthalm. suppl.* 2 (1933)

cal lagophthalmos during sleep (cf *Howitt et al*, who, however, used fluorescein alone and not rose bengal)

The rising frequency and intensity with increasing age may bear relation to the decreasing tear secretion and cornea wetting time (*Norn 1969 A*)

Rose bengal staining is an important *diagnostic aid in keratoconjunctivitis sicca*. It may even be claimed to be the most important diagnostic aid in practice because *Schirmer's* classical tear secretion test is unreliable. *Schirmer's* test gives pathological values in far too many normal eyes especially among elderly individuals (*Norn 1965*)

The 10 % rose bengal concentration is better suited to disclose the initial stage of keratoconjunctivitis sicca than the usually employed 1 % rose bengal. On the other hand the higher concentration will also disclose asymptomatic cases.

10 % rose bengal may thus give occasion to overdiagnosing of the sicca form while on the other hand using 1 % rose bengal one may fail to recognize mild attacks of this disease.

The 10 % rose bengal concentration may disclose pathological phenomena which are not detectable after instillation of 1 % rose bengal e.g. mild degrees of dendritic keratitis punctate keratitis corrosion etc.

A mixture of 1 % fluorescein and 1 % rose bengal is recommendable for routine staining. Fluorescein will then stain epithelial lesions and rose bengal degenerate epithelial cells (*Norn 1964 C*)

If no abnormality is detectable by this mixture supplementary vital staining with 10 % rose bengal may be undertaken. The latter vital-stain can disclose mild cases of dendritic keratitis adenovirus keratitis, corrosion keratoconjunctivitis sicca etc.

Summary

A total of 100 eyes had first 1 % rose bengal and thereafter 10 % rose bengal instilled.

The 10 % concentration stained more frequently and more intensely in all regions than the 1 %. Indirectly it was shown that 10 % rose bengal stains degenerate cells more intensely than trypan blue bromothymol blue and methylene blue.

In the normal eye degenerate epithelial cells were found peripherally below and nasally on the cornea and the adjacent part of the bulbar conjunctiva. (The cornea was stained in 40 and 77 per cent by 1 % and 10 % rose bengal respectively and the bulbar conjunctiva in 67 and 99 per cent)

Prof A Nover Mainz Der Augenhintergrund Untersuchungstechnik und typische Befunde. 2nd enlarged and revised edition Schattauer Stuttgart 1969 116 pages 148 figures (of this 108 figs in colour) Price DM 42-

This book is intended as an easily accessible manual giving clear pictures as an aid in assessing ophthalmoscopic findings and it may be emphasized at once that it certainly fulfils its purpose. It is unusually well planned, written in a lucid style and illustrated by a series of successful photographs of the fundus which demonstrate the various conditions better than a versatile description.

In spite of the limited number of pages this book contains a surprising abundance of details and differential diagnostic discussions.

It may be earnestly recommended, especially to students and general practitioners and for that matter also to ophthalmologists who want an aid in ophthalmoscopic diagnosis at a reasonable price.

Jens Edmund

Bradley R Straatsma Michael O Hall Raymond A Allen and Frederick Crescutelli The Retina - Morphology Function and Clinical Characteristics UCLA Forum Medical Sciences No 8 University of California Press Los Angeles pp 616

This comprehensive and informative volume contains the proceedings of the conference held November 1966 in connection with the opening of the Jules Stein Eye Institute University of California Los Angeles. The amount of knowledge presented by experts is certainly impressive and of the highest standard.

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P Brandstrup

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Bedrossian E Howard The Surgical and Non surgical Management of Strabismus
C C Thomas Springfield Illinois 1969 224 pages 70 figures Price \$ 11 50

At present this is one of the most useful books for ophthalmologists and ophthalmologists to be who are looking for down to earth and practical knowledge about their squint patients. All relevant aspects are presented in a clear concise and easily accessible manner. Anatomy physiology neurology method of examination non surgical and surgical treatment are given one chapter each. Moreover the book contains a chapter relating and defining the nomenclature.

The book is extremely didactic and at the same time gives sober assessment of the present possibilities and limitations of strabismus therapy. It is stressed for instance that the therapeutic results in accommodative esotropia are better with spectacles than with miotics and that nearly always it is impossible to cure a really fixed abnormal retinal correspondence. This is a book which may be earnestly recommended to all who want easily accessible useful sober and sufficient knowledge within the difficult field made up by our numerous squint patients.

E Gregersen

Hafferl Anton Lehrbuch der topographischen Anatomie neu bearbeitet von Walter Thiel 3rd edition pp 971 661 illustrations Springer Berlin Heidelberg New York 1969

This topographical anatomy including the international Paris Nomina Anatomica is extremely comprehensive. The section on the orbit and orbital region counts 34 pages and appears well suited for students. For post graduate teaching of ophthalmologists to be however it is too short. As it concerns only topography the ophthalmologist will moreover miss the gross and microscopic anatomy of the eye and eyelids etc.

Therefore the book cannot be recommended to ophthalmologists or ophthalmologists to be.

S Ry Andersen

Milauskas A T Diagnosis and Management of Blowout Fractures of the Orbit
Charles C Thomas Springfield Illinois 147 pages price \$ 8 50

A diagnosis of blowout fractures – downward displacement of part of the orbital floor unassociated with any damage to the margin of the orbit surrounding the facial bones presupposes a close collaboration between radiologist and ophthalmologist. Five out of the 8 chapters of this book are devoted to an accurate description of the radiological technique which may be used with most success paying particular attention to extra conal orbitography and polytomography (hypocycloid tomography) amply illustrated. Moreover a brief but sufficient clinical description is rendered with a clear presentation of the indications for surgery and the surgical technique. This book will afford good support in arriving at the correct diagnosis of blowout fracture.

Knud Norshov

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P Brandstrup

Campinchi R Faure P J Bloch Michel E and Haut J L Uveite Phenomenes immunologiques et allergiques Publication de la Societe française d'Ophthalmologie. Paris Masson & Co 1970 Pg 913

This year's report to the French Ophthalmological Society is as usual a very elaborate up to date presentation. The subject is uveitis. Of considerable value is the informing compilation of the present experimental data of the immunopathology of uveitis comprising the first 239 pages. A special immunological dictionary of 20 pages is found in the end of the volume. Clinical manifestations, diagnostic procedures, etiology and therapy are dealt with exemplarily and didactically arranged.

P Brandstrup

Illustrated Tumor Nomenclature/Nomenclature illustree des Tumeurs/Illustrierte Tumornomenklatur 2nd revised edition. Prepared by H Hamperl and L V Ackerman (Title, contents and preface in English, French, Russian, German and Spanish; legends also in Latin). Springer Verlag, Berlin Heidelberg New York. With 270 figures. 1969. 283 pages. 4to. 1969. Cloth DM 58.-

The object of this book is to provide illustrations of common neoplasms as they manifest themselves in the various organs, and at the same time the most widely accepted term for the tumour concerned. It has been endeavoured to avoid overlapping with the programme which is being developed by WHO and which is to result in a uniform histopathological nomenclature for tumours.

Some of the illustrations have been borrowed from the various fascicles of the Tumour Atlas of the Armed Forces Institute of Pathology, but often appear to be poorer than the originals, mainly because of a reduced size. On the whole, the tumours are illustrated by fairly typical pictures, although there are exceptions, also in the technical quality of the photographs.

All illustrations are black and white, but since they are to illustrate morphology, this is mostly an advantage. The choice of nomenclature does not appear to be at all appropriate, for instance in the case of the eye, where only 2 types are mentioned, viz. *diktyoma*, which is certainly not common, and *retinoblastoma*. *Diktyoma* is called *medulloepithelioma of ciliary epithelium*, which is unfortunate, as it may occur, though rarely, outside the ciliary body. *Retinoblastoma* is divided into two types, viz. with true rosettes and without true rosettes. This too is unfortunate, as in the same tumour different areas may exhibit from none to numerous rosettes and all transitions. The distinction is unnecessary and old-fashioned.

The book is of no interest to ophthalmologists, but may afford some help to the pathologist as a means of rapid reference, filling the gap until the WHO series has been completed.

O A Jensen

VARIA

The IV Congress of the European Ophthalmological Society

will be held in Budapest from 17th till 21st April 1962 under the presidency of Mrs. Professor M Radnot. The only topics to be discussed are the functional examinations in ophthalmology. For all information please write to Mrs. Professor M. Radnot, I Eye Clinic, University Medical School VIII Ilcz u 15 Budapest, Hungary.

International Council of Ophthalmology and International Federation of Ophthalmological Societies

The International Council of Ophthalmology and the International Federation of Ophthalmological Societies met in Mexico at the occasion of the XXI International Congress of Ophthalmology (7-14 March 1960). After having heard a report of Prof Streiff, Prof Nordmann, Dr Cuendet and Dr Schellhorn on the information of Ophthalmology they accepted a perforated card for the international coding system of eye disorders.

Concerning the contact lenses they accepted the following motion: "The indication, the prescription, the clinical and optical adaptation and the control of contact lenses must remain medical acts of which only the ophthalmologist has to assume the responsibility. Non medical technicians, even specialized in optics, may only participate in the optical adaptation as paramedical assistants in the doctor's office. These assistants have to be submitted to all the restrictions fixed by the regulations concerning the medical auxiliaries."

They also accepted criteria for the standardization of tonometers.

They nominated a committee for review and study of the visual standards for driving as adopted by the American Medical Association Committee of medical aspects of automotive safety.

Paris has been chosen as the place of the XXII International Congress of Ophthalmology (1964).

The Ophthalmological Societies of Iraq, Bolivia, Thailand, Morocco, Lebanon and the Asia Pacific Academy of Ophthalmology have been elected members of the International Federation.

Prof Bregeat, Dr Moutinho, Prof Hilton Rocha, Prof Sautter, Mrs Prof Vannas, Dr Stephen Miller and Dr Hogan have been elected members of the International Council of Ophthalmology.

Prof Jules François (Ghent) has been elected president of the International Council of Ophthalmology and of the International Federation of Ophthalmological Societies. Dr M Hogan (San Francisco) vice president, Prof Streiff (Lausanne) treasurer and Prof A Dubois Poulsen (Paris) secretary.

XIX SCANDINAVIAN OPHTHALMOLOGICAL CONGRESS

Bergen 1969

Address by the president of the Congress, Professor Torstein Bertelsen,
M D Bergen, Norway

Ladies and Gentlemen,

It is a great pleasure to welcome so many of my colleagues and their relatives from all the Northern countries, to the 19th Congress of Scandinavian Ophthalmologists. As probably most of you know, the first meeting was convened in Stockholm in June, 1900. Some of the proceedings of this meeting and also parts of the 5th Congress in 1921 took place in Uppsala. Apart from this the meetings were held in their entirety in the Capitals until 1954, the year of the 13th Congress. The University of Gothenburg had recently been opened and partly to mark this event the Congress was arranged in this town.

For the first time in Norway a Congress is now arranged outside the Capital. The reason for this decision is the same as in the case of the Gothenburg Congress.

The idea of a university in Bergen is of a long standing, but it was not until 1946 that it became a reality. The main factors forcing the foundation was the accumulation of prospective students during the war years and the increasing demand for academically trained people and in particular for doctors. From a very modest beginning when only a few students were admitted each year the University has expanded immensely and now it opens its doors to more than 1000 new students each year. About 80 of these are admitted to the Faculty of Medicine and this number will increase in pace with the expansion of the University Hospital.

Other new universities have been founded in the Nordic countries, in Umeå, Uleåborg and Odense and more will come in the near future. Let us hope that some of the future meetings of the Nordic ophthalmologists will be convened in these new university towns. I think this might be a very valuable stimulation to the new faculties.

By the time of the 1954 Congress the number of participants and lecturers had become so great that it was necessary to divide the meeting into two sections in order to get through the programme. This was far from an ideal solution and in 1965 it was decided to have only one section. To achieve this meetings should be convened every other year.

instead of the previous practise of every third year or even less frequent. The proceedings should be concentrated on a limited number of main topics.

After consultations with the Societies of Ophthalmologists in the Nordic countries it was decided to choose Neuro Ophthalmology and The Orbit as the main subjects for this Congress. These two topics are however so closely interrelated that there has been doubt as to which topic some of the lectures belong.

Neuro ophthalmology is a subject which has developed in pace with the growing importance of neurology in general and neuro surgery in particular. It has become one of the main supporting subjects in these fields. In many places it is already well established as an ophthalmological sub-specialty. The growing number of head injuries mainly due to traffic accidents will certainly increase the importance of this subject, and it will be necessary to establish ophthalmological sections in most large eye departments.

Neither is the orbit of interest only to the eye specialist. Many different pathological processes are capable of spreading to the orbit from adjacent organs, necessitating the close collaboration of specialists in several fields of medicine. In addition to this we have the remarkable hormonal disturbances which presents a problem both to the specialist in internal medicine and to the ophthalmologist.

Our two main subjects show clearly the central position held by ophthalmology in practical medicine, and it is pleasing to see that the problems will be approached from so many different points of view.

A number of lectures on subjects outside the two main topics have also been notified. I consider it important that especially the young ophthalmologists can find in the Scandinavian Congresses a forum where they are allowed to put forward the results of their research, to discuss them with others, to hear opposing points of view, and to be exposed to criticism. I am glad that we not have had to refuse any of these.

Dr Enoksson and Professor Ehlers, two of our colleagues who have been engaged to a very great degree in work on problems related to neuro ophthalmology and the orbit, have agreed to give the introductory lectures on these main topics. I take this opportunity of thanking them for the very considerable amount of work they have done in this connection.

I should also like to express my gratitude to my fellowmembers in the Congress Committee, headed by the secretary general, Dr Henry Aasved, for the interest and enthusiasm they have shown in preparing this meeting.

The Committee has taken the liberty of electing the following chairmen for the individual sessions. Professors Gunnar von Bahr, Poul Brændstrup,

Forstein Bertelsen, Holger Ehlers, Henrik Forsius, Viggo Jensen and Borge Lavatz, Dr Bengt Nyquist Professors Birger Malling Erik Palm, Bengt Rosengren, Henrik Sjogren, Dr Kristjan Sveinsson Professors Thore Thomassen and Jan Ytteborg

Since the last meeting our countries have lost several very capable and highly esteemed colleagues

From Denmark

Holger Hoff and Arne Jessen

From Finland

Lauri Kananen and Sigurd Werner

From Sweden

Ulf Wasen

From Norway

Johan Fredrik Harboe and Kristian Gilje

We Honour their Memory

I hereby declare the 19th Congress of Scandinavian Ophthalmologists open

THE ORBIT—A SURVEY

By

Holger Ehlers

It is with gratitude but hesitation too I have undertaken the honourable task to open discussion on orbital diseases. My scruples are due to the fact that the task in reality is insoluble. Concerning each group of diseases in this field is already written books. Others are written on exophthalmometry, tonography, angiography, pneumography, pisometry and others again on orbital surgery. Problems are so many and so different that nobody can master them all. More than a survey in broad outlines cannot be expected.

Before I present this survey it is reasonable to recall some peculiar anatomical and physiological features which characterize the orbit and therefore must be of influence on our conception of orbital pathology.

The orbit has most space in its anterior part. In the top posteriorly the space is very restricted. All increase in content has to get its way forward and here the bulb is placed as a valve or a piston which may be displaced. Acting to the rear is the pressure of the atmosphere, the eyelids and the pull of the rectus muscles. Forward acting is mainly the intra-orbital pressure as the pull of the oblique muscles owing to their slanting course only have a slight component forward.

The volume of the orbit is 35 cm^3 of this a little more than 7 occupied of the bulb. Then 28 cm^3 are left for muscles, nerves, fat tissue, glands and blood. Especially the amount of blood must be remembered as the veins in the orbit are many and form a soft pad for the bulb. By his interesting measurements P. M. Møller found the normal intraorbital pressure $30 \text{ mm H}_2\text{O}$ and this pressure was rather constant during various conditions if only the bulb was mobile. If the bulb was fixed, orbital pressure until $220 \text{ mm H}_2\text{O}$ was measured.

If P. M. Møller compressed the content of the orbit by a gradual pressure on a contact lens placed on the bulb the pressure in the orbit stayed rather unchanged until a compression of 6 mm . But then the

absence of lymph vessels in the orbit This may explain some of the characteristic reactions of the orbital tissue especially the ability for edema

The orbit is naturally divided in two parts the region inside the muscle-cone and the part outside Pathological processes inside the muscle cone produce an axial proptosis Processes outside the muscle cone produce displacement of the bulb in the frontal plane Space taking processes in the orbit may exert a pressure on the bulb A pressure from the rear may change the refraction several dioptries in hypermetropic direction Pressure against the bulb in the anterior part of the orbit may cause astigmatism of the cornea Ophthalmoscopically the pressure on the bulb may be seen as line white lines, sometimes in concentric formations Such marks may persist for months even if the pressing tumor is removed Pressure on the optic nerve may cause papillary edema, choked disc or atrophy followed by loss of vision

In the osseous walls of the orbit there are holes through which nerves and vessels pass in Processes in these passages are accompanied by characteristic symptoms dependent on the anatomy and assembled in syndroms Originally French authors put forward a 'Syndrome de sommet de l'orbite' Later on more differentiated syndroms are proposed

Canalis opticus loss of vision Ophthalmoscopic and roentgenologic changes

Fissura orbitalis superior 1 trigeminal is affected with neuralgias and disturbances of sensibility in its region The three motoric nerves may be affected although not with equal frequency A grouping of the symptoms in a medial and a lateral has been proposed

Fissura orbitalis inferior 2 trigeminal nerve may be affected Godfredsen found by tumors in the rhino-pharynx even symptoms from the Eustachian tube or the nasal cavity

Sinus cavernosus is placed so near the apex of the orbit that orbital symptoms are frequent The abducens nerve and the oculomotorius nerve are very exposed, the ophthalmic nerve too Vascular symptoms are pronounced (for instance anterior venous communication with pulsating exoftalmos and following subjectively and objectively perceived sounds)

In spite of the real orbital tissue only represents 20 gr and only $\frac{1}{3}$ of the weight of the body Its pathology is multitudinous and covers nearly all chapters of the pathology No other tissue elsewhere in the body seems to present so many manifestations from malformations inflammation and circulatory disturbances to haematopoiesis endocrinology and lipodystrophy It is peculiar that the morphology and chemistry of the orbital tissue is dependent on hormonal factors Cells fibrils and amor

pressure rose abruptly, presumably because the veins were compressed and the bloodpad empty. As the volume of a cone is $\frac{1}{3}\pi r^2 h$ the normal amount of blood in the orbit may be approximately 9 or 10 cm³. Bulb and blood together then represent nearly halfpart at the content of the orbit.

By attraction of the bulb forward by means of suction on a contact lens P. M. Møller measured a pronounced reduction at the intra orbital pressure. Owing to the conic form of the orbit a protrusion of 1 mm represented a much greater increase in volume than the diminution by 1 mm's enophthalmos. The scale of our exophthalmometers should in reality have registered volumes.

The orbital fat is a peculiar tissue. It is nice lobulated, mobile and easy to displace. Its amounts do not directly follow the fat deposits elsewhere. It reminds in structure of the subsynovial tissue around the joints preventing vacuum during movements. Under edematous conditions the lobulated orbital fat tissue loses its mobility and the movements of the eye are prevented in a pronounced degree. A simple orbital edema may in a purely mechanical way produce severe "pseudophthalmoplegia". The nerves and muscles may be intact. In elderly persons the orbital fat owing to the pressure in the orbit may be pressed forward through holes in the orbital septum forming the so called "adiposites orbitopalpebrales". The orbital fat seldom protrudes in the intervals between the recti muscles and become visible as "epibulbar lipoma".

Something fundamental in photography is that the apparatus is quite motionless in the moment of release, the same must hold good of the eye. How the pulse wave is prevented from asserting itself in the osseous limited space is not quite clear, but one or other hindrance there must be. In oftalmometry no pulsation of the bulb is visible. In tonometry a pulsation is visible when a weight rests on the eye. In his first mentioned measurement P. M. Møller could not register pulse synchronic variations in his curves for the pressure in the orbit. In some way the pulse is restrained. Probably the damper is to be found in the presence of so many veins, perhaps the peculiar feature of cavernous sinus play a part. Krakau and Bynke in their interesting registration of the ocular pulse put a weight of 20 grammes on the eye. The ipsilateral pulsations is dependent on the passage in carotis and a slight compression could produce a marked reduction. In the presense of Krakau, Bynke and Horven I have not more to say concerning ocular pulsation.

The many veins in the orbit are without valves and their outflow may pass posteriorly (to sinus cavernosus), anteriorly (to vena angularis) or downwards (to plexus pterygoideus). In spite of these abundant possibilities for the outflow, venous stasis can occur. A peculiarity is the

Chronic

Granulomatous

Boeck, Hodgkin

Pseudotumor

Parasites (Coccidia) fungus

Special

Tenonitis

Scleritis post

Traumatic

Contusions, Hematoma

Incisions, Stabs

Fractures

Lamina papyracea (emphysema)

Canal optic (atrophy)

Zygomatic (enophthalmos)

Blow out (to sin max)

Luxations

Shotlesions (toys, hunting suicide)

Foreign bodies (traffic, industry)

Vascular

Arterial

Angioma circoid

Aneurysma

Arteritis temporalis

Capillar

Angioma

Venous

Varices

Stasis orbitæ

Aseptic thrombosis

Cavernous angioma

Arterio-venous anastomosis

Pulsating exophthalmos

Systemic diseases

Endocrine

Thyreotoxic hypophysary

Osteopathic

Premature synostosis

Exostosis endostosis

phous substances take part in the changes. The cause of orbital alterations may be found far away, as for instance in Horner's syndrome.

The principal symptom in orbital diseases is exophthalmos. In spite of refined methods, among which Davanger's and Tengroth's exophthalmometry, it is still an intricate thing. Normal values are difficult to fix and variations considerable, for instance Knudtzon's and Bertelsen's. Often the clinical estimate is decisive. Here asymmetry of the skull must not be forgotten, neither unilateral myopia. According to Bertelsen, myopia, especially without myopic conus may resemble a proptosis. Paralysis of the recti muscles may cause a proptosis too.

A few words may be spent on unilateral and bilateral exophthalmos. After all they represent two quite different groups of diseases. Indeed it shall be admitted, that a bilateral case may start unilateral, but as a principal rule it can be stated that bilateral proptosis indicates a systemic disease and a unilateral a local disease.

The mysterious condition called "Pseudotumor of the orbit" has been discussed often. Either a tumor has disappeared spontaneously or a supposed tumor could not be found after orbitotomy. Presumably different conditions may cause a pseudotumor, for instance insidious inflammations, aseptic thrombosis or a systemic disease.

According to the system here set up the orbital diseases are divided in 7 groups. Some diseases could properly be placed in other groups as well. I hope you will find this survey of use.

Malformations

Microphthalmic orbital aplasia
Cyclopia
Cryptophthalmos
Orbito palbral cysts
Dental cysts
Dermoid cysts
Meningo encephalocele
Muscle defects

Inflammations

Acute

Odema	}	face
Periostitis		nasal sinus
Abscess		from teeth
Phlegmon		ear
Thrombophlebit		focal

- Fig 7* Dental cyst congenital
Fig 8 Dental cyst congenital
Fig 9 Teeth anlag in orbit
Fig 10 Axial exoftalmos
Fig 11 Deplaced exoftalmos
Fig 12 Deplaced granuloma orbit
Fig 13 Oxycephalia
Fig 14 Orbit enlarged
Fig 14 Orbit enlarged
Fig 16 Destruction of orbital wall
Fig 17 Enlarged fissura sup
Fig 18 Cribrum orbitae
Fig 19 Thyreotoxic exoftalmos
Fig 20 Melanoma orbitae child
Fig 21 Recklinghausentumor child
Fig 22 Recklinghausentumor adult
Fig 23 Lymfocytom upwards
Fig 24 Lymfocytoma downwards
Fig 25 Pressure of tumor
Fig 26 Pressure of tumor
Fig 27 Tumor retrobulb (choked disc)
Fig 28 Tumor retrobulb atrophy
Fig 29 Tumor retrobulb pressure
Fig 30 Abscessus orbit
Fig 31 Thrombophebitis
Fig 32 Angioma
Fig 33 Mucocoele
Fig 34 Exoftalmos pulsans
Fig 35 Meningeom
Fig 36 Meningeom
Fig 37 Endoftalmusitis exoftalmos
Fig 38 Thrombosed orbital veins
Fig 39 Thrombosed orbital veins

Leucæmic
 Plasmacytoma, lymphocytoma
 lymphatic infiltrations
 Lipodystrophic
 Liponecrosis
 lipogranuloma
 Neurogenic
 Recklinghausens disease
 Horner's syndrome

Tumors

Primary
 Fibroma, Lipoma, Myoma, Myxoma
 Sarcoma, Lipoma
 Reticulosarcoma
 Tumeur mixte
 Secondary
 Meningeoma
 Ghoma, Melanosarcoma
 Carcinoma (from lacrymal app.)
 Ghoma, Sarcoma from optic n.
 From neighbourhood
 Lids, nose, rhinopharynx
 Metastatic
 Carcinoma
 Neuroblastoma

Miscellany

Reticuloendothelioma
 Eosinophilic osteogranuloma
 Letterer-Siwe disease
 Hand-Schüller-Christian's disease
 Juvenile Xanthogranuloma
 Granuloma malignum
 (Wegener's «midline»)
 Cribra orbitalia

Following slides from the collection of the university eye clinic, Copenhagen were demonstrated

Fig 1 Hernia adiposa palpebræ
 Fig 2 Atrophia orbitæ infantilis
 Fig 3 Atrophia orbitæ infantilis

Fig 4 Atrophia orbitæ infantilis
 Fig 5 Cystis orbitæ
 Fig 6 Cystis orbitæ

From the Department of Ophthalmology, Sodersjukhuset, Stockholm Sweden

NEURO-OPHTHALMOLOGY A REVIEW

By

Paul Enoksson

Albrecht von Graefe (Fig 1) is the outstanding figure in modern clinical neuro ophthalmology. He introduced systematic plotting of visual field defects, gave the correct interpretation of the lesion underlying homonymous hemianopia and was the first to explore the eye ground with the ophthalmoscope invented by *Helmholtz* (1851). *Von Graefe* suggested that a choked disc indicates intracranial tumour (14) and described its transition into optic atrophy in a style which seems unsurpassed in lucidity and accuracy (Fig 2).

The development of clinical neuro ophthalmology has been intimately related to the increasing knowledge of the anatomy of the visual pathway. Renaissance artists had a detailed knowledge of muscular anatomy, but when *Leonardo da Vinci* (Fig 3) in his "Quaderni d Anatomia" sketched his concept of the human visual system he was still swayed by medieval misinterpretations. He drew a hollow optic nerve connected to three vesicles of the brain, a *cellula phantastica* for perception, a *cellula logica* for thinking, and a *cellula memorialis* for memory (Fig 4). This was all the more remarkable as *Leonardo* is known to have performed careful dissections of the cerebral ventricles.

Now we possess a detailed knowledge of the architecture of the visual system, but we should make it clear to ourselves that this knowledge is in many respects of recent date. As late as the turn of the century two schools with prominent members fiercely discussed the problem as to whether an exact topographical representation of the visual fields exists in the occipital lobe. The most famous advocate of the hypothesis assuming a diffuse representation in the cortex was *Constantin von Monakow* (Fig 5) in Zurich, known for his demonstration of the lateral geniculate bodies as important parts of the visual pathway. To the rival school belonged the German ophthalmologist *Hermann Wilbrand* (Fig 6), who cooperated with the neurologist *A. Saenger* in preparing the encyclopedic work "Die



Fig 5
Constantin von Monakow (1853-1930)

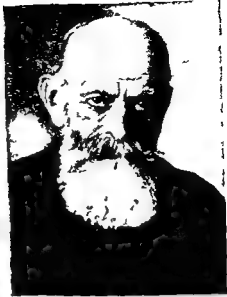


Fig 6
Hermann Wilbrand (1851-1935)

Neurologie des Auges in ten volumes(29) *Wilbrand* once had the opportunity to examine a patient with left sided narrow horizontal homonymous scotomas (Fig 7) When the patient died *Wilbrand* sent the fixated brain to another famous champion of the idea that there is a point for point representation of the visual field in the occipital cortex, the Swedish neurologist *Salomon Henschen* (Fig 8) The latter found a vascular lesion restricted to the floor of the right calcarine fissure(15) He drew the conclusion that here was the representation of the visual field surrounding the horizontal meridian

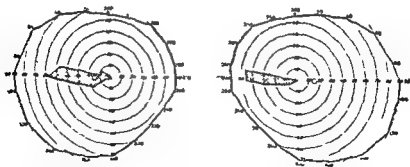


Fig 7

The case of *Wilbrand Henschen* with horizontal homonymous scotomas caused by vascular lesion of the right calcarine fissure (*Wilbrand & Saenger 1917*)



Fig 3
Leonardo da Vinci (1452-1519) Self
portrait

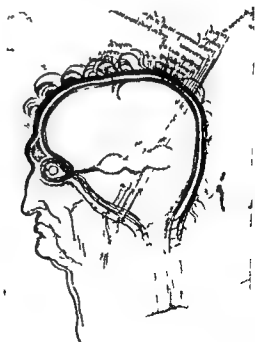


Fig 4
From Leonardo da Vinci's : Quaderni
d Anatomia

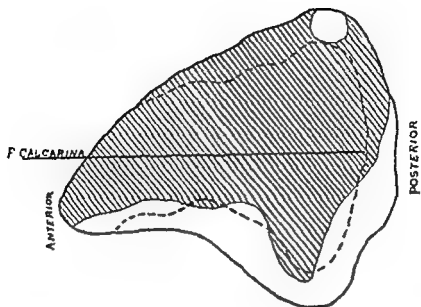


Fig 11

Right area striata in the case of Holmes. The portions destroyed by softening are shaded (Holmes 1934) Cf Fig 10

case of bilateral vascular lesions of the calcarine cortex which is of interest when compared with the case of *Wilbrand Henschen* (17). The only parts of the visual fields preserved in this case were wedge shaped remnants along the upper vertical meridian down to and including the fixation area (Fig 10). Postmortem examination showed superficial cortical softening of the striate area except only for the peripheral parts of the lower calcarine lip and the rearmost part of the visual cortex (Fig 11). The horizontal meridian of the visual fields is thus represented at the floor of the calcarine fissure and the vertical meridian peripherally.

The pioneer work of *Harvey Cushing* (Fig 12) included almost every field of neurosurgery. He played an important part in the practical application of perimetry in topical neurological diagnosis. At Johns Hopkins Hospital in Baltimore *Cushing* was once visited by the anatomist *Adolf Meyer*. A study of the secondary degeneration following vascular and traumatic lesions of the brain had convinced *Meyer* that the ventral part of the geniculo-calcarine pathway turns forward along the temporal horn before it runs backward towards the visual cortex (Fig 13). If this conception was right — and it was in accordance with the findings of *Flechsig* in myelogenetic studies — temporal lobe lesions might yield restricted homonymous field defects. In *Cushing's* clinic there happened to be a man with a left temporal lobe lesion caused by a bullet which had passed



Fig 8

Salomon Henschen (1847-1930)



Fig 9

Gordon Holmes (1876-1963)

During the first world war the English neurologist *Gordon Holmes* (Fig 9) served as a consulting neurologist to the British Expeditionary Force in France. He studied in detail the visual fields in several cases of gunshot wounds of the head and made important contributions to our present conception of the topography in the striate area. *Holmes* also described a

left eye

right eye

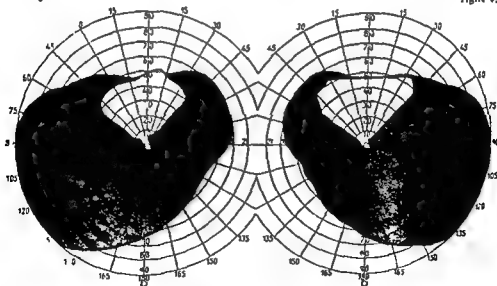


Fig 10

The case of *Holmes* with wedge shaped remnants of the visual fields along the upper vertical meridians (*Holmes* 1934) Cf Fig 11

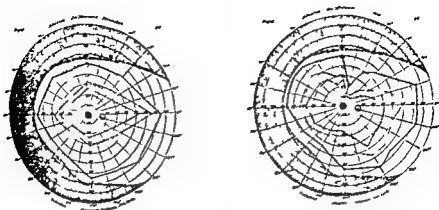


Fig 14

The case of Cushing with traumatic lesion of left temporal lobe Left visual field of right eye on admission of the patient Right visual field re-examined at the suggestion of Adolf Meyer (Cushing 1922)

upper segmental defect to the right of the vertical was recorded (Fig 14) and though in this case the field of the other eye could not be examined, the homonymous upper quadrantanopia this important sign of temporal lobe damage was discovered in principle

In 1912 Cushing published his monograph on the pituitary body and its disorders(8) The same year he persuaded a young doctor, Clifford B Walker, to join the staff for the purpose of working on ophthalmological problems This proved important for the development of perimetric technique at the clinic(27) Compared with the modern Goldmann perimeter Walker's instruments may seem primitive (Fig 15) but his investigations left nothing to be desired as far as accuracy and scientific critique are concerned Colour interlacing (Fig 16) had formerly been considered a reliable sign of increased intracranial pressure at Cushing's clinic but Walker showed that there is no warrant for this concept(26)

However, we do not have to look outside Europe or even Scandinavia to find a brilliant representative of quantitative perimetry at this time Henning Ronne (Fig 17) He also performed an important study on the structure of the lateral geniculate nucleus(25)

Supplementary information about the architecture of the visual system has been provided up to the very last years The elegant studies of Hoyt & Luis are of special interest in two technical respects Like earlier investigators they studied the secondary degeneration of the optic nerves and chiasm following retinal injury This was not, however produced in a crude mechanical way but with the aid of a Zeiss photocoagulator Nor did they study the degeneration by the indirect method of Marchi but by the silver impregnation technique of Vauta & Gygar which makes the de

Fig 12
Harvey Cushing (1869-1939)



through the left eye and had lodged in the petrous portion of the left temporal bone(9) One of *Cushing's* assistants had examined the right visual field as a matter of routine on the patient's admission to hospital. He had not expected any defects and had not found any. At *Meyer's* suggestion perimetry was repeated and additional meridians were now explored. An

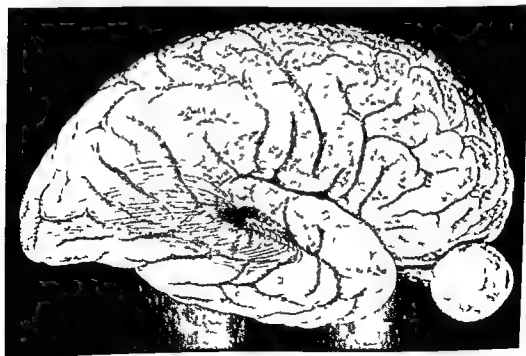


Fig 13
Visual pathway in man drawn by Max Brodel (*Cushing* 1922)



Fig 17
Henning Rønne (1878-1947)

generating axons themselves visible(19) *Hoyt* found that the arcuate fibres of the retina remain as intact units throughout the optic nerves (Fig 18) and also for a short distance after having entered the chiasm(18) *Hoyt & Luis* made beautiful reconstructions of the fibre tracts inside the chiasm, exemplified in Fig 19 which shows how macular fibres are distributed



Fig 18
The course of the arcuate retinal fibres in the left optic nerve chiasm and optic tracts of the monkey (*Hoyt 1967*)



Fig 15
A perimeter of Clifford Walker's (Walker, 1916)

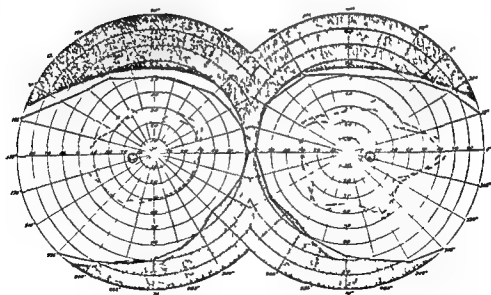


Fig 16
Colour interlacing in the right field once thought to be a sign of increased intra-cranial pressure (Walker 1916)



Fig 17
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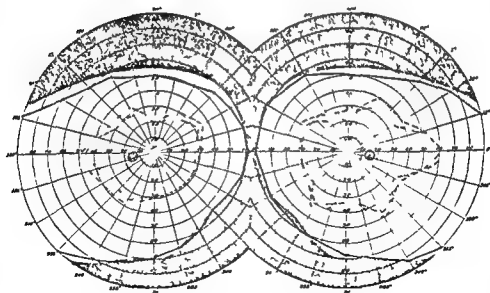


Fig 16
Colour interlacing in the right field once thought to be a sign of increased intra cranial pressure (Walker 1916)

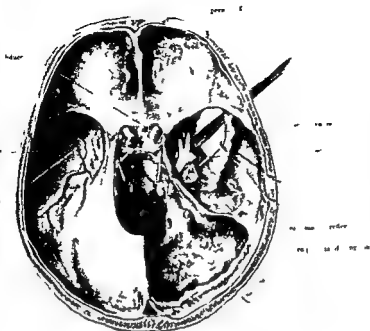


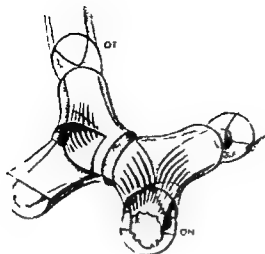
Fig. 21

A neurosurgical approach to the Gasserian ganglion sketch performed by Harvey Cushing (Cushing 1900)

If the ophthalmologist wants to make himself familiar with the clinically important neuro anatomical facts he should not forget to visit the neurosurgical operating theatre. Excellent operative sketches can be found in the works of Cushing, e.g. in his monograph: Meningiomas written together with the neuro pathologist Louise Eisenhardt and published in 1938 a year before Cushing's death (10). Fig. 21 shows a drawing by Cushing demonstrating an approach to the Gasserian ganglion, drawn at a time (1900) when the ganglion was still extirpated in cases of trigeminal neuralgia (7). Apart from the topography of the ganglion it shows other anatomical details of ophthalmological interest. The oculomotor nerve can be seen penetrating the dura between the free and attached borders of the tentorium cerebelli a location where it may be compressed in herniation of the brain. The abducens nerve can be followed passing freely through the cavernous sinus. This course of the nerve explains why abducens palsy is an early sign of malignant nasopharyngeal tumours penetrating the base of the skull a fact which has been amply verified in the monograph of Godfredsen (13). The position of the abducens nerve is still better seen in Fig. 22 which is taken from a publication of D. Parkinson,

Fig 19

Macular projections through the primate
chiasm (Hoyt & Laus 1963)



over the major part of the chiasm. The crossing macular fibres do not form small separate bundles at the posterior angle of the chiasm as maintained in many text books.

Almost every fact concerning the structure of the visual system known up to 1955 was presented this year in a monumental work by *Stephen Polyak* (Fig 20), born in Yugoslavia, medically educated in Austria and finally working as professor in Chicago. He devoted almost thirty years of his life to 'The Vertebrate Visual System', a beautiful book which is still an indispensable source of knowledge(24). Its 10,000 references suggest the dimension of the work.



Fig 20

Stephen Polyak (1889-1955)



Fig 23

Walter Edward Dandy (1886-1946)



Fig 24

Ewald Hering (1834-1918)

eyes, Gesetz der gleichmassigen Innervation beider Augen (16) He founded a famous school for physiologists To this belonged *Alfred Bielschowsky* (Fig 25) who left Europe for America in 1936 He played an important role in his new country, promoting the study of disturbances in



Fig 25

Alfred Bielschowsky (1871-1940)

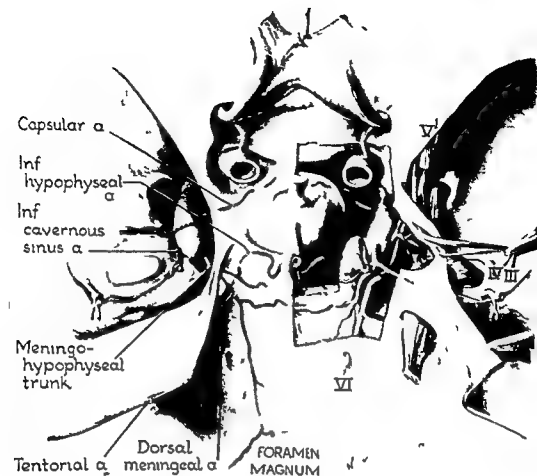


Fig 22

The anatomy of the cavernous sinus (Parkinson, 1965)

the drawing being based on experience of more than 200 cavernous carotid dissections. These were performed in order to find a surgical approach to this part of the internal carotid artery(23)

The importance of *Cushing* to the development of clinical neuro ophthalmology has been mentioned already(12). Great contributions were also made by the other neurosurgical genius of America, *Walter Edward Dandy* (Fig 23), who was also responsible for epoch making progress in neuro roentgenology by devising the methods of ventriculography and encephalography. In 1921 he described his transcranial surgical approach in the treatment of orbital tumours(11). This was a great step forward as these tumours are often partly intraorbital and partly intracranial.

A detailed knowledge of anatomical facts is indispensable for topical diagnosis. Physiology, on the other hand, has taught the ophthalmologist to understand many of the symptoms and signs which he will meet in neurological cases. *Ewald Hering* (Fig 24), brilliant contemporary of *Helmholtz*, formulated the fundamental law of equal innervation to both

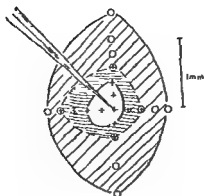


Fig 28
Receptive field of a retinal ganglion cell (Kuffler 1953)

In 1953 *Stephen Kuffler* succeeded in recording potentials from separate ganglion cells in the retina by means of microelectrodes (Fig 28) These were introduced into the eye of the cat in such manner that the eye remained otherwise intact and could be stimulated physiologically(22) This technique was epoch making It was utilized and further developed by *Hubel & Wiesel*, who extended their study to the geniculate bodies and the visual cortex(20,21) Their research has revealed fundamental facts concerning the analysing function of the striate area In columns of cells perpendicular to the surface of the brain *Hubel & Wiesel* recorded maximal response only with a special field orientation (Figs 29 and 30) They also found cells of different ocular dominance ranging from wholly contralateral to strongly ipsilateral

In 1963 *Carpenter et al* reported the strange observation that discrete lesions of the abducens nucleus in the monkey not only produced abducens palsy but rather a paralysis of the ipsilateral conjugate horizontal gaze (Fig 31) Searching previous literature in this field they found the phenomenon already described in man(6) In 1889 two English neurologists, *Bennett & Savill*, had reported a case of paralysis of conjugate ocular movements to the left(1) Autopsy revealed a minute patch of softening in the left abducens nucleus (Fig 32)

Dante Alighieri unexpectedly meets his admired teacher *Brunetto Latino* in the fire rain of *Inferno* When they part company, *Latino* urgently advises his former pupil

Steti raccomandato al mio Tesoro

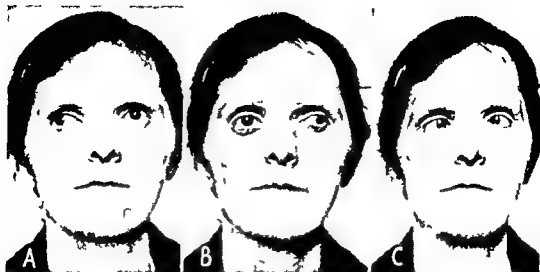


Fig 26
Internuclear ophthalmoplegia (Bielschowsky, 1939)

ocular motility(2,3) In Scandinavia his name is perhaps most intimately connected with the description of internuclear ophthalmoplegia (Fig 26)

1952 is an important year in the history of neuro ophthalmology. This year Åke Björk introduced his technique (Fig 27) of electromyographical examination of the human extraocular muscles(4,5)



Fig 27
Electromyographical examination of the internal rectus muscle (Björk 1955)

- horizontal eye movements in the monkey I Physiological effects and anatomical degeneration resulting from lesions of the abducens nucleus and nerve Arch. Neurol 1963 8 231-247
- 7 Cushing H A method of total extirpation of the Gasserian ganglion for trigeminal neuralgia By a route through the temporal fossa and beneath the middle meningeal artery J Amer med Ass. 1900 34 1035-1041
 - 8 Cushing H The Pituitary Body and its Disorders Philadelphia J B Lippincott Co 1912 341 pp
 - 9 Cushing H Distortions of the visual fields in cases of brain tumour — The field defects produced by temporal lobe lesions Brain 1922 44 341-396
 - 10 Cushing H and Eisenhardt L Meningiomas — Their classification, regional behaviour life history and surgical end results Reprint New York Hafner Publishing Co 1962 785 pp
 - 11 Dandy W E Orbital Tumors — Results following the transcranial operative attack London H K Lewis & Co 1942 168 pp
 - 12 Fulton J F Harvey Cushing — a biography Springfield Ill Charles C Thomas 1946 754 pp
 - 13 Godtfredsen E Ophthalmologic and Neurologic Symptoms at Malignant Nasopharyngeal Tumours — A clinical study comprising 454 cases Copenhagen E Munksgaard 1944 323 pp
 - 14 Graefe A von Ueber Complication von Schnervenentzündung mit Gehirnkrankheiten Graefe Arch Ophthal 1860 7 Abt 2 58-71
 - 15 Henschen S E Über circumscribte Nutritionsgebiete im Occipitallappen und ihre Bedeutung für die Lehre vom Sehzentrum Graefe Arch Ophthal 1911 78 195-211
 - 16 Hering E Der Raumsinn und die Bewegungen des Auges in Handbuch der Physiologie der Sinnesorgane ed. by L Hermann Leipzig F C W Vogel 1879 vol 3 part 1 343-601
 - 17 Holmes G The representation of the nasal sectors of the retinae in the calcarine cortex Jahrb f Psychiat u Neurol 1934 51 39-48 Reprinted in Selected Papers of Sir Gordon Holmes Compiled and ed by F M R. Walshe London Macmillan & Co 1956 pp 195-203
 - 18 Hoyt W F Anatomic considerations of arcuate scotomas associated with lesions of the optic nerve and chiasm — A Nauta axon degeneration study in the monkey Johns Hopk Hosp Bull 1962 111 57-71
 - 19 Hoyt W F and Lusk O The primate chiasm — Details of visual fiber organization studied by silver impregnation techniques A M A Arch Ophthal 1963 70 69-85
 - 20 Hubel D H The visual cortex of the brain Scientific American 1963 (Nov) 209 54-62
 - 21 Hubel D H and Wiesel T N Receptive fields binocular interaction and functional architecture in the cat's visual cortex J Physiol 1962 160 106-154
 - 22 Affer S B Discharge patterns and functional organization of mammalian retina J Neurophysiol 1953 16 37-68
 - 23 Parkinson D A surgical approach to the cavernous portion of the carotid artery — Anatomical studies and case report J Neurosurg 1965 23 474-483
 - 24 Polyak S The Vertebrate Visual System Ed. by H Kluver Chicago University of Chicago Press 1957 1390 pp
 - 25 Rönne H Den Menneskelige Synsbanes Arkitektur København E Munksgaard 1942 50 pp



Fig 33
Frank B Walsh

Frank B Walsh (Fig 33) could give the same advice to the ophthalmologists of the world. His "Clinical Neuro-Ophthalmology" is a real Tesoro, a treasury, an almost inexhaustible mine of neuro ophthalmological information(28)

REFERENCES

- 1 *Bennett A H and Savill, T* A case of permanent conjugate deviation of the eyes and head, the result of a lesion limited to the sixth nucleus with remarks on associated lateral movements of the eyeballs and rotation of the head and neck *Brain*, 1889 12 102-116
- 2 *Bielschowsky A* Lectures on motor anomalies IX Oculomotor nerve paralysis and ophthalmoplegias *Amer J Ophthal* 1939 22 484-498
- 3 *Bielschowsky A* Lectures on Motor Anomalies Dartmouth publications 1956 186 pp
- 4 *Bjork A* Electrical activity of human extrinsic eye muscles *Experientia* 1952 8 226-227
- 5 *Bjork, A* Elektromyografiska studier av de yttre ögonmusklerna hos människa Stockholm P A Norstedt & söner 1955 24 pp
- 6 *Carpenter M B, McMasters R E and Hanna G R* Disturbances of conjugate

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ORBITAL PHLEBOGRAPHY

By

Ivar Paul Enge and Bjørn Bergaust

Dejean and Boudet introduced orbital phlebography in 1951 (4) Together with *Palairac and Bouhieres*(2) they also studied the topographic anatomy and the pathologic conditions of the orbital veins Most recently a number of publications on the subject of orbital phlebography have appeared (1378) From a diagnostic point of view it has been stated that the superior ophthalmic vein is the most important orbital vessel This is due to the almost symmetrical appearance of this vein with its extension about 20 millimetres within the muscle cone in close relation to the optic nerve Thus expansive lesions especially those originating from within the muscle cone or from the orbital roof may result in dislocation, distortion or compression of the vein In addition diseases in the veins proper such as varices and occlusions may be directly demonstrated

The patients presenting with unilateral exophthalmos often constitute a difficult diagnostic problem This report describes the use of orbital phlebography in 25 such patients

Technique

A modified percutaneous transfrontal approach(8) was used in 22 patients In 2 cases percutaneous puncture of the angular vein(8) was performed and in 1 further case we applied the internal jugular vein technique (3 5)

The patient is placed in Trendelenburg's position One of the midline forehead veins then usually may be seen or palpated The vein is punctured with a scalp vein needle gauge 19 or 21 to which a polyethylenetubing filled with normal saline is attached 10 millilitres of Isopaque 350 are injected by hand as rapidly as possible At the same time the patient compresses both anterior facial veins with his index fingers against the maxillary bone Most of the studies were performed on a skull table unit,

- 26 *Walker, C B* Color interlacing and perimetry *Trans Amer Ophthal Soc*, 1916, 14 684-718
- 27 *Walker C B* Quantitative perimetry, practical devices and errors *Trans Amer Ophthal Soc*, 1917, 15 166-193 and *Arch Ophthal (N Y)*, 1917 46 537-561
- 28 *Walsh, F B* *Clinical Neuro Ophthalmology* Baltimore Williams & Wilkins Co, 1957, 2nd ed 1294 pp
- 29 *Wilbrand, H and Saenger A* *Die Neurologie des Auges* Vol 7 *Die homonyme Hemianopsie nebst ihren Beziehungen zu den anderen cerebralen Herderscheinungen* Wiesbaden J F Bergmann 1917 608 pp

Fig 2
Slight asymmetria Expansion in anterior
part of the right orbit? Inconclusive finding



be considered as definitive evidence of pathology since slight asymmetria may occur in normals

Case 2 Haemangioma of the orbit Verified by carotid angiography and operation

Phlebogram (Figure 3) Obvious asymmetria with medial displacement of the right superior ophthalmic vein The angles of the 'vein parallelo-



Fig 3

Obvious asymmetria Distortion of the right orbital vein parallelogram due to a haemangioma

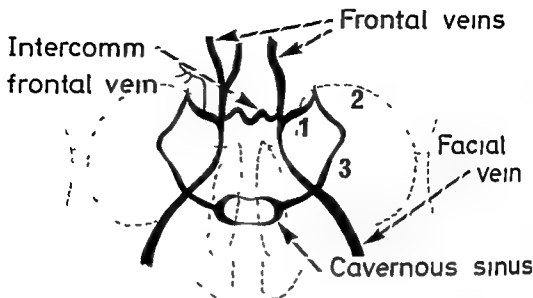


Fig 1

Schematic drawing of normal orbital phlebogram as seen in a 15° submento-occipital view

one exposure made before the start of injection and one at the end of injection of the contrast medium, thus making the subtraction technique possible (3). A 15 degrees submento occipital projection has been the standard view. In only a few instances lateral projection was used. In a few cases a serial film changer was used.

Result and case reports

In 25 patients 27 orbital phlebographies were performed. Successful puncture and adequate visualization of the orbital veins were obtained in 20 patients. Definitive pathology was revealed in 10 patients, while in 7 cases no abnormality was detected in the orbital phlebogram. Inconclusive findings were found in 3 patients. Due to difficulties in puncturing the vein, the studies were incomplete in 5 patients.

The radiological findings in some of the cases are briefly presented in the following. Figure 1 shows a schematic drawing of a normal orbital venogram as seen in a 15 degrees submento occipital view. The different segments of the superior ophthalmic vein and its communications anteriorly and posteriorly are demonstrated.

Case 1 Slight exophthalmos on the right side. No final diagnosis has been reached as yet in this case.

Phlebogram (Figure 2) Slight medial and distal displacement of the 1 and 2 segments of the right superior ophthalmic vein. This finding cannot



Fig 5

Distortion and partly nonfilling of left orbital vein parallelagram Optic nerve gloma (arrow see text)

shown a vascular expansion, probably haemangioma and small arterio venous shunts

Phlebogram (Figure 6) Angular vein puncture — subtraction picture Complete lack of filling of posterior $\frac{2}{3}$ of the left superior ophthalmic vein Some distortion dislocation widening and unsharp demarcation posteriorly of the filled part of the vein, most probably due both to compression from the expansive mass and existing arteriovenous shunts with increased venous pressure

Case 6 Mucocoele of the left frontal sinus Verified by operation

Phlebogram (Figure 7) Distal and lateral dislocation of the 1 and 2 segments of the left superior ophthalmic vein caused by the mucocoele expanding through the bone defect in the orbital roof

Comments

Orbital phlebography can be carried out utilizing a simple technique and conventional roentgen equipment The examination has no complications and the side effects are reduced to the discomfort accompanying



Fig 4

Nonfilling of the 2 and 3 segment of left superior ophthalmic vein. Dislocation and distortion of supra orbital vein branches (arrows). Bone defect in orbital roof. Dermoid cyst.

gram" decreased, indicating expansive lesion outside the muscle cone (8-9). Case 3: Dermoid cyst of the left orbit. Verified by operation.

Phlebogram (Figure 4): Only the first segment of the left superior ophthalmic vein is visualized. Considerable distortion and dislocation of the supra orbital vein branches (arrows). A bone defect in the orbital roof is seen.

Case 4: Optic nerve glioma of the left orbit. Verified by operation.

Phlebogram (Figure 5): Non filling of the posterior part (3 segment) of the left superior ophthalmic vein. Slight elevation of the 2 segment and increased angle between this and the 3 segment (indicating expansive lesion within the muscle cone), and a "tapering down" appearance on the junction to the nonfilled part (arrow) probably due to compression of the vein from outside.

Case 5: Tumour of the left orbit. Exophthalmos progressing through a period of 20 years. No definitive histological diagnosis has been established as yet in this case. Internal carotid angiography left side has

the puncture of the vein and a temporary burning sensation in the orbital regions during and shortly after the injection of the contrast medium. The method was originally confined to disease of the orbital veins proper in which the study is elective. However, as demonstrated in recent papers from other clinics, we also have found that orbital phlebography gives valuable information in the evaluation and assessment of expansive lesions of the orbit.

REFERENCES

1. Aron Rosa D and Offret G. La Phlebographie orbitaire. Bull. Soc. Fr. Ophtal. Supplementum 1967.
2. Belouhiers P, Palerac R, Boudet C. First results of phlebography. J. Radiol. Electrol. 34 1953 160-165.
3. Dayton G O and Hanafce W V. Orbital Venography. In Surgery of The Orbit. Amer. J. Ophthal. 67 1969 512-519.
4. Deyan C and Boudet C. Du diagnostic des varices de l'orbite et de leur complications par la phlebographie. Bull. Soc. Franc. Ophtal. 64 1951 374-377.
5. Hanafce W V, Shiu P C and Dayton G O. Orbital Venography. Amer. J. Roentgenol. 104 1968 29-35.
6. Lombardi G. Radiology in Neuro-Ophthalmology. Williams & Williams, Baltimore 1967.
7. Lombardi G and Passerini A. Venography of the orbit: pathology. Br. J. Radiol. 42 1969 184-188.
8. McNulty J G. Phlebography of the orbital venous system and the cavernous sinus. Br. J. Radiol. 42 1969 113-121.
9. Schöber R and Bender R. Orbita Phlebographie. Fortschr. Röntgenstr. 109 1968 345-360.



Fig 6

Angular vein puncture Subtraction picture Slowgrowing vascular expansion with small arterio venous shunts on the left side Nonfilling of posterior part of the vein due to the expansion and the A V shunts



Fig 7

Dislocation of the veins due to mucocoele originating from the left frontal sinus



Fig 1

Dermoid cyst of right orbit. Diminished size of right orbit and area of diminished density of bone. Sickie shaped density at margins (arrow)

small vessels (Dilenge and Fischgold 1963) By angiography aneurysms, vascular tumours and malformations are readily shown, and expanding lesions of the orbit may cause vascular displacement. The ophthalmic artery has a rather tortuous course however and there are many anatomical variations in the pattern and the distribution of vessels. Accordingly tumours in the orbit must be of a considerable size to cause vascular displacement recognizable on the arteriograms. Pathological vessels may sometimes be seen in the tumour area. Roentgenanatomical investigations have elucidated the normal arteriographic image, and the relation between the ophthalmic artery and the optic nerve (Dilenge *et al* 1965). The following three segments are usually well recognized in the arteriograms:

- 1 Initial segment
 - 2 Optical lateral segment
 - 3 Supra optic segment
- (Figures 2a and b)

1 The initial segment consists of an intracranial portion (a) 3-6 mm long, an intracanalicular portion (b), marked by a slight narrowing of

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RADIOLOGIC EXAMINATION IN ORBITAL TUMOUR

By

Bjørn Bergaust and Ivar Paul Enge

Plain X ray films are important in orbital tumours. Indicative and sometimes conclusive results may be obtained with manifestations in the bone (Hartmann and Gilles 1959). Diagnosis of type of tumour is possible in some groups of tumours. Glioma of the optic nerve, meningioma of the sphenoidal ridge, osteoma, tumour of the paranasal sinuses and dermoid cysts. According to Pfeiffer and Nicholl (1948), dermoids may be distinguished from other causes of proptosis by the characteristic roentgenographic appearance. The lesion of the bone is that of an area of diminished density with smooth, regular margins of increased density of bone at the margin.

Case 1 A 70 years old man with unilateral proptosis of more than 20 years duration presents a typical case of a dermoid cyst of the orbit (Figure 1). The dermoids probably develop from intradiploic germs, push the periosteum, and the elevation from the bone may cause the bone formation which is shown on the film as a sickle shaped density.

The application of contrast media in the radiological examination of orbital tumour augments the positive results, and new information as to the site, size and nature of the lesion, is added. The present contrast methods in orbital X ray are the phlebography, the ophthalmic arteriography and the orbitographies. Orbital phlebography is elective for the study of venous disease of the orbit, and also gives valuable information in the study of expansive lesion of the orbit. We have made this subject of a special paper (Engel and Bergaust 1970).

Filling of the ophthalmic artery occurs during carotid angiography in up to 98 per cent (Krayenbuhl 1962). The selective injection of contrast media into the internal carotid artery and rapid serial angiography are important for the visualization of the ophthalmic artery. The interpretation is facilitated by subtraction technique, improving the contrast of

Case 2 Aneurysm is clearly demonstrated in a case of a typical extra-dural aneurysm of the carotid siphon (Figure 3a) showing unilateral exophthalmos, papilledema, diminished vision and osseous destruction of the lesser and greater sphenoidal wings (Figure 3b)

Displacement of the arteries is demonstrated by the following two cases

Case 3 Glioma of the optic nerve of a 55 years old man caused an upward concave arch of the opticolateral segment and the intra-orbital portion of the initial segment and also a slight irregularity of the lumen (Figure 4)

Case 4 A great dermoid cyst of the orbit in a 40 years old man nearly filled the upper two thirds of the orbit and caused 8 mm proptosis, without any disturbance of vision. The ophthalmic artery was pushed backwards by the cyst, augmenting the tortuosity of the branches (Figure 5)

Case 5 Multiple pathological vessels are shown in a 68 years old woman who had unilateral exophthalmos and pulsating supra orbital tumour because of metastasis from a hypernephroma (Figure 6)

Orbitography may be done with positive or negative contrast media. Pneumo-orbito tomography, as described by Bertelsen (1956, 1957, 1960, 1962 and 1966) using air as a negative contrast medium, is our standard method. Tomography is done in lateral and frontal position. Providing adequate quantity of air is insufflated in the capsula of Tenon, within and outside the muscle cone and correct X ray exposure are used the orbital content is clearly demarcated. The negative contrast of air appears dark on an ordinary X ray film representing less radiologic density than the orbital content. In lateral position may thus be delineated the eye ball, the optic nerve and the muscle cone. In frontal view the eye ball and some of the ocular muscles are demarcated by air in Tenon's capsule. Frontal omograms through the muscle cone may produce sections of the optic nerve and the muscles as well. A soft tissue shadow in all pictures is seen to wall out the osseous orbit. Space occupying lesions may alter the orbito-pneumotomogram in several ways. Dislocations of the normal content, increase in the orbital soft tissue shadow and abnormal content delineated by air. The orbital expansion may be ill defined or the shape and size of a tumour may be more or less well defined by the air contrast.

Case 6 Glioma in a 5 years-old girl exhibiting proptosis, papilledema and vision 5/15 is demonstrated as a spindle shaped tumour of the optic nerve. Figures 7a and b)

Case 7 (same patient as case 4) A great dermoid cyst is delineated by air and the exact localization, shape and size of the cyst were known prior to surgery (Figure 8)



(a) Arteriogram Vide text for explanation



(b) Drawing made from the arteriogram

Fig 2
Ophthalmic artery lateral view

the lumen, and an intraorbital portion (c) which is mostly about 10 mm long, being inferior and lateral to the optic nerve

2 The opticolateral segment makes a sharp bend before taking an upward direction. After a subsequent turn it runs for a short distance above the optic nerve. This turn is not always detectable on the films

3 Then the artery leaves the nerve to enter the medial part of the orbit as the supraoptic segment

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Case 6 Glioma in a 3 years old girl exhibiting proptosis papilledema and vision 5/15 is demonstrated as a spindle shaped tumour of the optic nerve (Figures 7a and b)

Case 7 (same patient as case 4) A great dermoid cyst is delineated by air and the exact localization shape and size of the cyst were known prior to surgery (Figure 8)



(a) Carotid angiography lateral view



(b) Destruction of sphenoidal wings (arrow)

Fig 3

Extradural aneurysm of carotid siphon



Fig 4

Gloma of optic nerve angiography lateral view Displacement of arteries (arrows)

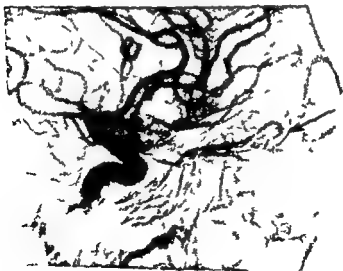


Fig 5

Gr at d m o d cyst angiography lateral view Ophthalmic artery pushed backwards. (arrow)



Fig 6

Metastatic hypernephroma selective arteriography of external carotid artery Destruction of bone and pathological vessels (arrows)

Positive contrast orbitography is used as a routine procedure by some (Lombardi 1967). Because of serious accidents reported (Dollfus) we prefer to do supplementary positive contrast medium examinations in cases of reduced vision only, and we have achieved conclusive result by this method when pneumoorbitotomography failed. 3-iodated water soluble contrast medium (Isopaque 260) is mixed with a similar quantity of a local anaesthetic (2 per cent Xylocain) and injected inside the muscle cone as for retrobulbar anaesthesia. The position of the needle radiologically assured, 3-5 ml of the mixture is injected. The cannula is left in position, and because of rapid elimination of contrast medium from the tissue, a few ml of contrast mixture is added during the tomography.

Case 8 (same patient as case 3). In the case of a glioma of the optic nerve, the air contrast method was inconclusive. The vision being finger counting at 20 cm, the positive contrast method was applied. Accidentally the cystlike glioma was punctured and dyed with positive contrast medium (Figure 9a and b).

X ray examinations with contrast media in our opinion are valuable diagnostic aid in the study of orbital tumour. We consider no method the



(a) Lateral view



(b) Frontal view

Fig 7

Glioma of optic nerve Orbitopneumotomography

method of choice, and we believe that the use of multiple methods do increase the positive results. Orbital phlebography and ophthalmic angiography can disclose lesions directly by showing pathologic vessels and indirectly by demonstrating vascular displacement. By orbitotomography the site and size of space-occupying lesions may be demonstrated. The result depends much upon the quality of the X ray films obtained.



Fig 8
Dermoid cyst, orbitopneumotomography, lateral view

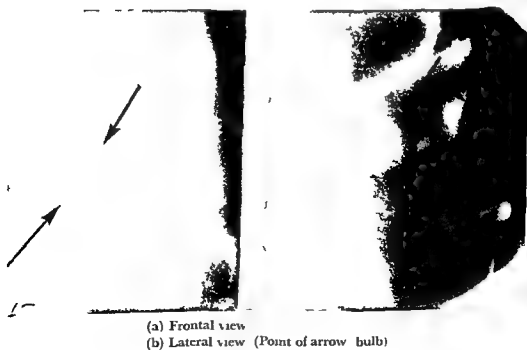


Fig 9
Cystlike gloma of optic nerve (arrows) positive contrast tomogram

Summary

Plain X ray films in orbital tumour may give indicative results and sometimes as in dermoid cysts conclusive results may appear. Usually radiologic contrast methods are necessary for the exact and early diagnosis of orbital tumours. Orbital phlebography, ophthalmic arteriography, negative and positive contrast-orbitotomography may all supply further information as to the shape, size, localization and nature of orbital lesions.

REFERENCES

- Bertelsen T I The use of radiographic contrast media in diagnosing orbital tumors. *Acta Ophth* 34 355 1956
- Bertelsen T I and Petersen O Orbital pneumography. *Acta Radiol* 47 426 1957
- Bertelsen T I A new and improved technique in orbital pneumography. *Acta ophth* 38 57 1960
- Bertelsen T I Pneumotomography of the orbit. *Arch Ophthal* 68 446 1962
- Bertelsen T I Diagnostische Methoden bei einseitigem Exophthalmus. *Ophthalmologica* 1515 309 1966
- Dileage D et Fischgold H L'angiographie orbitaire par voie carotidienne. *Ann Oculit* 196 29 1963
- Dollfus cit by Offret et al.
- Engel P and Bergaust B Orbital phlebography. *Acta ophth* (in press)
- Hartmann E and Gilles E Roentgenologic diagnosis in ophthalmology. J B Lippincott company Philadelphia Montreal 1959
- Krayenbuhl H The value of orbital angiography for diagnosis of unilateral exophthalmos. *J Neurosurg* 19 289 1962
- Lombardi G Radiology in neuro-ophthalmology. Baltimore Williams & Wilkins Co 1967
- Offret G Gilles E et Blanchot F De l'intérêt des tomographies orbitaires avec injection d'air en ophtalmologie. *Arch Ophthal (Paris)* 14 259 352 1954
- Pfeiffer H L and Nicholl R J Dermoids and epidermoids of the orbit. *Trans Am Ophth Soc* 46 218 1948



Fig 8

Dermoid cyst, orbitopneumotomography, lateral view

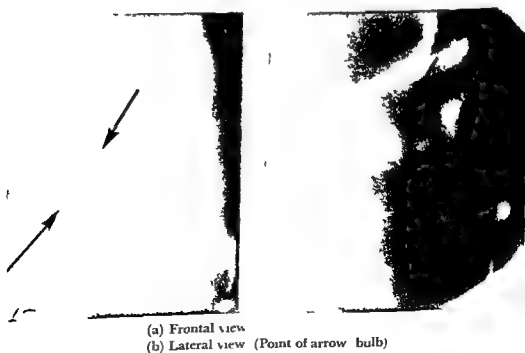


Fig 9

Cystlike glioma of optic nerve (arrows) positive contrast tomogram

outside the orbit are not included in this number. The table shows the diagnostic distribution of these 17 cases

Hemangioma	3
Optic nerve meningioma	2
Meningioma	1
Mixed tumour of lacr gl	1
Neurofibroma	1
Fibroma	1
Dermoid	1
Sarcoid	1
Pseudotumour	1
 Fibrosarcoma	 2
Osteosarcoma	1
Neurosarcoma	1
Malignant melanoma	1

One notices that 12 benign tumours have been allocated to 8 different histological varieties and 5 malignant ones have been labeled with 4 different diagnoses.

The hemangiomas are congenital tumours. They have, however, a tendency to grow and manifest themselves in adult life. The 3 patients represented here were all adults. Orbital hemangiomas in children often have a diffuse demarcation and are extremely vascular. The method of choice to achieve a definite diagnosis in this age group is therefore considered to be arteriography or venography (Bertelsen 1956). However, the cavernous hemangiomas which are found in adults are as a rule, sharply demarcated from the surrounding tissues. The vessels are partly thrombosed giving the tumour a firm elastic structure and the blood content and the perfusion rate are often so low that it is hard to diagnose by angiography.

In the literature there has been recorded a case where transient hemiplegia arose from injection of air into an orbital hemangioma (Dollfus 1953). Bottomly & al (1960) have presented a case where an orbital hemangioma was demonstrated by pneumography. The 3 hemangiomas in this study have all been demonstrated and diagnosed by pneumotomography without any sorts of complications.

Fig 1 is from a woman age 53 who presented with left-sided exophthalmos which had gradually developed over a period of 2½ years. The frontal view shows a tumourlike shadow above the eyeball and displacing this downwards (Fig 1 A). The tumour is circumscribed by

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ORBITAL PNEUMOTOMOGRAPHY

By

Torstein I Bertelsen

The diagnosis of the deep seated tumours of the orbit will as a rule have to rely upon X ray examinations. These examinations will usually have to be aided by some sort of artificial contrast. A positive contrast method may be employed using a radio opaque compound which is injected either intravascularly or directly into the orbital tissues, or a negative contrast is produced by insufflation of air.

This paper will summarise the cases of primary orbital tumours which has been treated at the eye department, Haukeland Sykehus, between 1962 and 1968. Special emphasis will be put upon the diagnostic value of orbital pneumotomography.

The technical part of this procedure has been dealt with in previous papers (Bertelsen 1960, 1962), but I would like to emphasize that relatively large quantities of air (15-20 cc) are required in order to obtain a good result, as a great deal of the air will escape into the eyelids. The air has to be deposited in several different positions in the orbit, especially within the capsule of Tenon and inside the muscle funnel but also in the more peripheral parts. I will also like to stress that reasonable results with this technic cannot be achieved unless the X ray equipment is able to produce serial tomograms where the distance between the sections are 5 mm or less.

The diagnosis of an expansive process in the orbit may rest on the fact that the growth either dislocate or deform the normal intraorbital structures as judged by the distribution of the shadows or the air will in fact outline the tumour by distributing itself on the tumour surface. Of course this is most often the case when the tumour is demarcated from the surrounding tissues by a capsule.

A total number of 5 711 patients were admitted to the eye department in the years 1962-68. 17 of these (0,3%) had space occupying lesion in the orbit.

Superficial dermoids and a few cases of metastatic deposits from tumours

outside the orbit are not included in this number. The table shows the diagnostic distribution of these 17 cases

Hemangioma	3
Optic nerve meningioma	2
Meningioma	1
Mixed tumour of lacr gl	1
Neurofibroma	1
Fibroma	1
Dermoid	1
Sarcoid	1
Pseudotumour	1
Fibrosarcoma	2
Osteosarcoma	1
Neurosarcoma	1
Malignant melanoma	1

One notices that 12 benign tumours have been allocated to 8 different histological varieties and 5 malignant ones have been labeled with 4 different diagnoses.

The hemangiomas are congenital tumours. They have, however, a tendency to grow and manifest themselves in adult life. The 3 patients represented here were all adults. Orbital hemangiomas in children often have a diffuse demarcation and are extremely vascular. The method of choice to achieve a definite diagnosis in this age group is therefore considered to be arteriography or venography (Bertelsen 1956). However, the cavernous hemangiomas which are found in adults are as a rule sharply demarcated from the surrounding tissues. The vessels are partly thrombosed giving the tumour a firm, elastic structure and the blood content and the perfusion rate are often so low that it is hard to diagnose by angiography.

In the literature there has been recorded a case where transient hemiplegia arose from injection of air into an orbital hemangioma (Dollfus 1953). Bottomly & al (1960) have presented a case where an orbital hemangioma was demonstrated by pneumography. The 3 hemangiomas in this study have all been demonstrated and diagnosed by pneumotomography without any sorts of complications.

Fig 1 is from a woman age 53 who presented with left-sided exophthalmos which had gradually developed over a period of 2½ years. The frontal view shows a tumourlike shadow above the eyeball and displacing this downwards (Fig 1 A). The tumour is circumscribed by

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ORBITAL PNEUMOTOMOGRAPHY

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Superficial dermoids and a few cases of metastatic deposits from tumours



Fig 2

Normal optic canals in woman aged 20 with rightsided meningioma of the optic nerve (Fig 3)

Fig 4, 5 and 6 belongs to a 4 year old boy. His mother suffered from typical neurofibromatosis. Our patient had no skin tumours, but many café au lait spots were noted. He presented with a slight rightsided exophthalmus which gradually developed during a quarter of a year and the vision was reduced on this eye to 5/15. Some degree of rightsided papilloedema was found, while the left eye was completely normal. A glioma of the optic nerve was suspected as this is often seen as a complication to neurofibromatosis. This type of tumour is considered to expand the optic canal more readily than the meningiomas (Craig & Gogela 1949). In our case the X ray examinations showed that both the optic canals were large (Fig 4) but with insignificant difference between the two sides. Pneumotomography (Fig 5) demonstrated



Fig 3

Pneumotomography in rightsided meningioma of the optic nerve. A Frontal section. B Sagittal section. Arrows points to the thickened optic nerve.



Fig 1

Pneumotomography in left-sided orbital hemangioma A Frontal section Arrows points to the tumour The eyeball is displaced downwards B Sagittal section Open arrows outline the tumour The small arrows points to the optic nerve

a thin layer of air The sideview section through the middle of the orbit demonstrates the tumour above and behind the globe (Fig 1 B) The optic nerve is displaced downwards By operation through lateral orbitotomy a circumscribed hemangioma was found, and this was removed without any difficulties

Tumours of the optic nerve are usually benign and they do not affect the very loose connection to the surrounding tissues which are characteristic of the normal nerve Air injected into the capsule of Tenon will easily spread along the surface of the nerve demonstrating any thickening These lesions therefore seems to be the ones which are most easily demonstrated by pneumotomography

Fig 2 and 3 belongs to a 20 year old woman The sight of the right eye gradually subsided to 5/10 during a two year period On examination a relative rightsided exophthalmus amounting to 2 mm was demonstrated Some degree of papilloedema and marked concentrically decreased visual field were also noted The left eye was completely normal, and a general neurological examination failed to reveal any pathology elsewhere A rightsided meningioma of the optic nerve was suspected, but an X-ray examination of the orbit and the optic canals (Fig 2) were normal A rightsided carotid angiography proved also negative Pneumotomography of the orbit (Fig 3) showed a definitely thickened optic nerve, the thickening extending as far forward as the bulbus The eye and the thickened optic nerve was removed Histological diagnosis was meningioma of the optic nerve

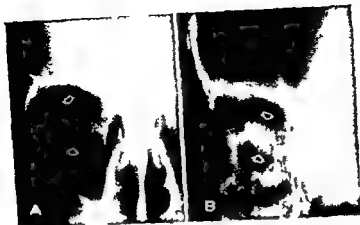


Fig 5

Pneumotomography in right-sided meningioma of the optic nerve A Frontal section B Sagittal section Arrows points to the enormously thickened optic nerve surrounded by air Note that the thickening tapers off both anterior and posterior to a near normal calibre

a 16 year old girl who in a course of two to three years had a gradually increasing exophthalmus and inferior deviation of the left globe X ray examination showed that the left orbital cavity was greatly enlarged upwards A left-sided carotid arteriography showed normal conditions Pneumotomography revealed in the frontal view that most of the upper part of the orbit seemed to be filled with a growth which displaced the bulbous downwards and flattened the upper part of the globe (Fig 7 A) A sagittal section through the middle part of the orbit showed the growth above and behind the bulbous (Fig 7 B) It can be seen that the tumour is distinctly separated from the globe and the optic nerve At lateral



Fig 6

Optic nerve meningioma in a boy with neurofibromatosis Left Section showing the optic nerve surrounded by tumour tissue Mallory X 15 Right Tumour tissue x 150 Insertion H P view showing psammoma bodies

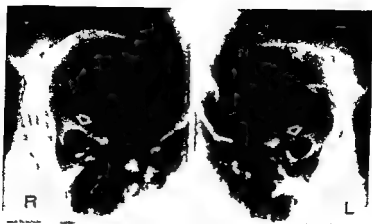


Fig 4

Optic canals in a boy aged 4 with neurofibromatosis and rightsided meningioma of the optic nerve (Figs 5 and 6) Both optic canals are large but the difference between them is insignificant

grossly thickened optic nerve both in the frontal and the lateral sections. The nerve seemed to have a normal size at the insertion into the bulbus and also in front of the optic canal. The nerve with the tumour was removed by lateral orbitotomy. Histological examination revealed that the tumour was not a glioma, but a meningioma (Fig 6). The two cut ends showed no tumour cells.*

Meningiomas can, however, appear in the orbit without any evident connection to the optic nerve or to the cranial cavity. One such case was seen in this study. Pneumotomography was not done in this case.

The mixed cell tumours will either originate from the lacrymal gland itself or from aberrant lacrymal tissue elsewhere in the orbit. The diagnosis of a mixed cell tumour is therefore not precluded by finding a tumour outside the normal site of the lacrymal gland. These tumours are usually well defined. I have shown in a previous paper that mixed tumours can be demonstrated by pneumotomography, (Bertelsen 1956), which also was the case in the patient included here.

Neurofibromas of the orbit may occur as isolated single lesions, or may be part of generalized neurofibromatosis. Our case had a solitary tumour. Pneumotomography was not carried out, but I have previously proved that such tumours also can be demonstrated by this method (Bertelsen 1960).

Dermoids are ususally superficial tumours, but occasionally they may be found deep in the orbit without any appearant connection to superficial structures. One such case was seen in our clinic. The patient was

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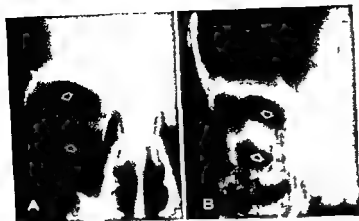


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Summary

Seventeen out of 5 711 patients (0 3%) referred to the eye department, Haukeland sykehus during a seven year period had primary tumours of the orbit. Pneumotomography of the orbit is a valuable and safe method in diagnosing these growths. This method gives the best results in benign, encapsulated tumours where the air can spread over the tumours surface. Tumours of the optic nerve seems to be the growth which is most easily demonstrated.

REFERENCES

- Bertelsen T I: The use of radiographic contrast media in diagnosing orbital tumours. *Acta Ophthal* 1956 34 355
- Bertelsen T I: A new and improved technique in orbital pneumography. *Acta Ophthal* 1960 38 57
- Bertelsen T I: Pneumotomography of the orbit. *Arch Ophthal* Chicago 1962 68 44
- B Henley S, Jarcho L W, Stowell D W & Chatterley J G: Unilateral exophthalmos. *Arch Ophthal* Chicago 1960 64 438
- Craig W M & Cogala L I: Intraorbital meningiomas. *Amer J Ophthal* 1949 32 1663
- Dollfus M A: Hemiplegie gauche transitoire au cours d'une injection d'air retrobulbaire pour exploration radiographique de l'orbite. *Bul Soc Ophth France* 1963 5 486

Discussion

Å Ehlers (Ålesund)

At Århus Kommunehospital we have attempted to diagnose intraorbital tumors by means of arteriography, venography and pneumotomography. In case of a big tumor the diagnosis is generally easy, with small tumors however often difficult.

Having observed the paper by Planol et al (Ann ocul Paris 1967 200 609) on portography we have used scanning with ^{125}I albumin and $\text{Tc}^{99\text{m}}$. Positive diagnosis has been obtained with $\text{Tc}^{99\text{m}}$. The method is quick and harmless to the patient.

H Gronnall (Kristianstad)

During a period of 26 years we have noted and gathered the reports of orbital tumours seen at the eye-department in Kristianstad Hospital. This Hospital treated 140 000 patients this period and the hospital serves a population of about $\frac{1}{2}$ of a million people.

The benign tumours were dominated by the dermoid cysts. Five of these were found inside the orbit, the others presented themselves on the orbital edges.

Two cavernous haemangiomas were removed through a Kronlein approach with unexpected little bleedings. The engorged cavernous cavities were separated by a connective tissue network infiltrated by round cells.

Two tumours were removed through a transfrontal approach by the neurosurgeon. One of these was a two years old girl who had an optic glioma without enlargement of the optic foramen and without the café au lait skin spots. The other case was a 60 years old man who presented with a fibroma with myxomatous degeneration. It produced an impression in the orbital roof which could be recognised by X ray examination.

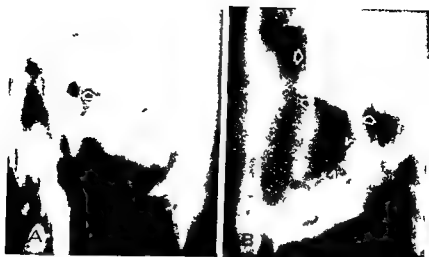


Fig 7

Pneumotomography in left-sided orbital dermoid A Frontal section The orbit is enlarged upwards The upper part of the orbit is filled with a soft mass which displaces the globe downwards and flattens its upper contour B Sagittal section Open arrows outline the mass Small arrows point to the optic nerve

orbitotomy one could remove a large dermoid which partly escaped into the temporal fossa through a defect in the lateral wall of the orbit

The diagnosis of *pseudotumour* was made in one single case This concerned a 45 year old man who for three years had pronounced right-sided exophthalmus and decreasing vision on this eye Orbital pneumotomography was carried out twice, but it failed to reveal any growth At operation one found a firm, elastic tissue mass with no distinct limitation in the deeper part of the orbit This explains the failure of localisation by pneumotomography

A rapidly increasing exophthalmus without signs of inflammation usually heralds a malignant process The four sarcomas in our series all showed this feature If the tumour is infiltrating the surrounding tissue as usually is the case, one would not expect to have much benefit from a pneumotomography All the four cases with sarcomas were children Pneumotomography was not carried out The malignant melanoma was found in a 42 year old woman who for a year and a half had a gradually increasing left-sided exophthalmus The findings on pneumotomography made us suspect a well limited and capsulated tumour in the superior part of the orbit At lateral orbitotomy one found, however, a diffusely limited tumour which could not be removed completely The histological diagnosis turned out to be malignant melanoma One could not demonstrate any connection between this tumour and tissues of the bulb of the eye or conjunctiva Likewise one could not find any other primary tumour Exenteration of the orbit was therefore performed a few days later

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REFERENCES

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- Bertelsen T I A new and improved technique in orbital pneumography *Acta Ophthal*
1960 38 57
- Bertelsen T I Pneumotomography of the orbit *Arch Ophthal* Chicago 1962 68 44
- Bottomley S Jarche L W Stouell D H & Chatterley J G Unilateral exophthalmos
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- Craig H M & Cogala L I Intraorbital meningiomas
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A 52 years old man had a xanthoma at a size of a walnut removed through an orbitomy. This intraorbital xanthoma was related to a small skinlesion in the upper eyelid. No X ray changes could be demonstrated. Histological examination of the specimen showed large fat and foam cells.

One meningioma has been found in the orbit who originated from the larger wing of the sphenoid bone, and one from the optic sheath.

A mixed tumour of the lacrimal gland has been removed inside its capsule by a Kronlein operation. The patient is still alive and he shows no signs of relapse 12 years after the operation. The histological examination showed a benign appearance with epithelial islands in a myxomatous matrix.

v Bahr described in 1938 the first case of an orbital Abrikosoffs myoblastomyoma. We had a case where the tumour was located near the orbital floor adjacent to the periosteum. Histological examination of the specimens showed a large syncytium with coarse acidophilic granulations.

A very rapid growing pseudotumour was removed three weeks after the first symptoms through an orbitomy. This granuloma was rich in giant cells.

Four cases of mucocoeles have been recorded.

Amongst the malignant tumours one would mention two cases with reticulocell sarcoma. In one case the point of origin was the nasale sinus and in the other the primary focus was located to tissue inside the orbit. In the latter case the total exenteration was carried out and in addition a series of X ray treatments were given. The tumour destroyed especially fat and muscle tissues. The patient has no sign of recurrence 9 years after the operation.

A 66 years old woman was operated on by the Kronlein method and inside the orbit we found a blue black, collapsed tumour and a total orbital evacuation followed. The patient died two years after the operation and she had a local recurrence of her malignant melanoma which grew to the size of a double fist. By re examining the original bulbous one found a very small peripheral malignant melanoma in the chorioid with scleral penetration.

Two cases of malignant lymphoma tumours have been referred to the radiotherapy department for treatment.

A five years old girl was admitted with a shallow tumour under the orbital roof. She presented with a severe anemia and changes in the bloodpicture resembling those of an acute myelogenous leucaemia. The patient died and a postmortem examination revealed a green coloured chloroma. The histological examination showed the same immature myeloid leucaemic changes as were demonstrated in her spleen and in the bonemarrow.

H. H. Seedorff (Copenhagen)

The contributor points out the advantage of the positive contrast method which has been carried out on 60 patients at Rigshospitalet, Copenhagen. Two illustrations were shown: 1. hygroma from the frontal sinus and 2. tumor of the lacrimal gland.

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PRINCIPLES AND SOURCES OF ERROR IN EXOPHTHALMOMETRY A NEW EXOPHTHALMOMETER

By

Martin Davanger

The purpose of exophthalmometry is to produce a numerical measure of the position of the eye in the orbit. This measure is used from three different points of view

1 In *absolute* exophthalmometry the result is compared with a known normal value

2 In *comparative* exophthalmometry the results are compared from time to time

3 In *relative* exophthalmometry the result is compared with the measure from the other eye in the same person

Reference points in exophthalmometry

A numerical measure of the position of the eye in the orbit is based upon the definition of two reference points: one point on *bulbus oculi*, and another point on the cranium. A measurable relation between the two points must be stated.

The natural reference point on the eye ball is *apex corneae*. The other reference point on the cranium has been less evident. Cohn (1865) who constructed the first exophthalmometer used originally the lateral orbital margin as reference. It is interesting to note that he later considered this point as frequently asymmetric in relation to an ideal plane vertical through both *processus mastoidei*. This brought him two years later to construct a new exophthalmometer with this the *superior* orbital margin was used as reference (Cohn 1867).

Several other reference points have been proposed (see Drews 1957), but the reference point in general use is still the deepest point on the lateral orbital margin. This point will be used as reference in the following.

It is important to remember that the exophthalmometric value indicates the relation between *two* points. The so-called fixed reference point on the lateral orbital margin may also vary in its position. This is prob-

ably an important cause of the wide scatter in the exophthalmometric value found in normal people, from 11 to 24 mm. Pathological variations of the position of the lateral orbital margin should be considered both in absolute exophthalmometry (e.g. in anomalies of the cranial growth), in relative exophthalmometry (e.g. in facial asymmetry), and in comparative exophthalmometry (e.g. after fractures and operations influencing the position of the orbital margin).

The simple distance between the two reference points cannot be used as a measure of the position of the eye. Most exophthalmometers measure the distance from apex corneae to a frontal plane through the deepest point on the lateral orbital margin.

In practice there are two different ways of defining this frontal plane, and accordingly we have two different types of exophthalmometers. The first type is simply a ruler, which alternately is placed on right and left side (Example Luedde's exophthalmometer (Luedde 1938)). This type measures from a frontal plane which is parallel with what must be called 'the facial plane'. The frontal plane is placed at discretion.

The other type has two rulers which are placed on both sides at the same time (example Hertel's exophthalmometer (Hertel 1905)). With this type is measured with reference to a frontal plane defined by two points, namely the deepest point on the lateral orbital margin on right and left side.

If the two lateral orbital margins have a symmetrical position, a frontal plane defined according to the first method coincides with a frontal plane after the other definition. However, in asymmetry the result of exophthalmometry depends on which one of the two principles has been used. This may be of practical importance especially in comparative exophthalmometry.

Technical problems in exophthalmometry

In exophthalmometry the following technical problems are faced.

- 1 The zero point of the scale must be placed on the frontal plane described.
- 2 The scale must be held horizontal in a sagittal plane.
- 3 Apex corneae must be projected to the scale without parallax.
- 4 An exact reading of the projection of apex corneae on the scale must be obtained.

We will see how these problems are tackled in some types of exophthalmometers in general use. For each point some sources of error will be mentioned.

The position of the zero point. Some exophthalmometers are simply a modified ruler, and the scale is placed alternately on the patient's right and left side. In principle, it is quite simple to place the zero point of the

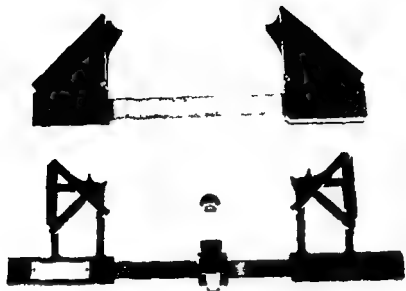


Fig 1

The Hertel exophthalmometer (Keeler) below and a mirror exophthalmometer (Oculus) above

scale in the right position on the lateral orbital margin. On the other hand some exophthalmometers of this type are inaccurately made so that the end of the ruler does not represent the zero point of the scale.

In the other type of exophthalmometers the Hertel type, in which the scale is placed on both sides at the same time the problem of placing the scale's zero point in the right position is not quite simple. The important point is the design of the exophthalmometer's footplate on the lateral orbital margin.

Fig 1 shows two widely used exophthalmometers the Hertel exophthalmometer (Keeler's) below and a mirror exophthalmometer made by Oculus above. In this connection we are especially interested in the form of the exophthalmometer's footplate on the orbital margin. The profile is a circle arc. In Oculus exophthalmometer the arc is obliquely set and has a radius of 85 mm. There is no point on the footplate to show the position corresponding to the zero point on the scale that is where the orbital margin should be placed. The position of the orbital margin in the relation to the footplate depends on the distance set between the two halves of the exophthalmometer. By using the instrument it will be found that the right distance is not evident to illustrate this the exophthalmometer was set 5 times in succession on the same person, and the

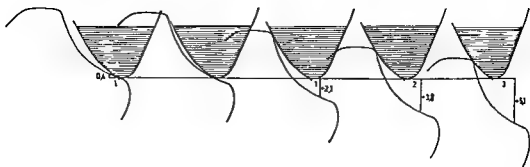


Fig 2

The effect of the position of the exophthalmometer's footplate in relation to the orbital margin

distance varied between 111 and 116 mm. The resulting displacement of the footplate in relation to the orbital margin influences the measure to a considerable degree, as can be seen in figure 2. The error caused by the displacement was measured as seen in the figure (the profile of the footplate and a cast of the lateral orbital margin was magnified 10 times in the original figure). It is demonstrated that, e.g., a 2 mm displacement medially will have the effect that the result will be 3.8 mm higher than the correct value.

The direction of the scale. Exophthalmometers of the Luedde type do not give an adequate solution to the problem of setting the scale in a sagittal plane. The ruler is placed at discretion, and a certain degree of deviation is probable. The reading is supposed to be performed in a direction at a right angle to the scale, and a deviation will introduce an error λ which may be calculated (Figure 3) from the equation $\lambda = e - e' = a \tan \alpha \cos \pi \pm (1 - \cos \alpha)e$, where e is the correct exophthalmometric value, e' is the value which will be measured when the scale deviates an angle π from the sagittal plane, a is the distance from apex corneae to a sagittal

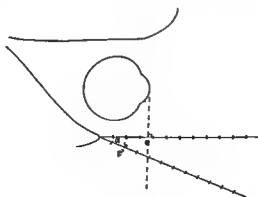


Fig 3

The effect of a deviation of the scale from the sagittal plane

plane through lateral orbital margin (the + sign is used when the scale deviates from the median plane, the - sign when the scale deviates towards the median plane)

The size of the error, as calculated from the equation for some values of c and a is given in table 1 ($a = 20$ mm (Hertel 1905))

Table 1

c	-10	-5	+5	+10
8mm	+3.4mm	+1.7mm	-1.8mm	-3.6mm
18mm	+3.2mm	+1.7mm	-1.8mm	-3.7mm
28mm	+3.0mm	+1.6mm	-1.8mm	-3.9mm

It will be seen from the table that if the ruler deviates 5° in one reading, and 5° in the other direction in the next reading a difference based on this error of 3.5 mm will be obtained. This is of course serious, especially in relative and comparative exophthalmometry.

The parallax error in exophthalmometry The distance between apex corneae and the scale is at least 15–20 mm, and a right angled projection is then of course decisive.

In Luedde's exophthalmometer a projection at a right angle is meant to be obtained by using *two* scales one on each side of the Perspex ruler, which is 8 mm thick. When the relevant lines on the two scales coincide the projection should be right.

This principle is adequate, but it has been found that the scales are not placed sufficiently accurately on the ruler. Seven different Luedde's exophthalmometers have been measured and it was found that the deviation introduced by the relative position of the scales varied between 4.5 and 0.6. The parallax error x caused by the deviation may be calculated from the equation $x/b = \tan \alpha$ (see Figure 4)



Fig 4

The effect of inaccuracy in the position of the two scales in relation to each other

In table 2 is shown the deviation measured and the resulting calculated error in the exophthalmometric measure for each of the seven exophthalmometers ($b=24$ mm in 1 position (i.e. the scale is facing the observer, and $b=16$ mm in 2 position (i.e. the scale turns the other way)) The error has also been measured more directly on a simple model, the results of this are also given in table 2

Table 2

	Deviation	Calculated error		Difference	Measured difference
No 1	4,5	+1 87mm	-1,25mm	3,1mm	3 0mm
No 2	3,3	+1 38mm	-0,92mm	2,3mm	2,1mm
No 3	3,0	+1 26mm	-0 84mm	2,1mm	1 7mm
No 4	-2,3	-0 96mm	+0,64mm	1 6mm	2,0mm
No 5	-1,7	-0 70mm	+0 47mm	1 2mm	1 2mm
No 6	1 2	+0 49mm	-0 33mm	0 8mm	0 9mm
No 7	0 6	+0 24mm	-0 16mm	0 4mm	0,1mm

In Hertel's exophthalmometer the problem of parallax is tackled in a peculiar way, which is best understood by analysing the original model, which was described in 1905 (Hertel 1905) The scale is placed in a frontal plane through the patient's temporal region (Figure 5) Cornea is seen in profile by the help of a mirror placed at 45° from the lateral orbital margin. By this arrangement apex corneae can be seen projected against the scale. If the direction of sight (dotted line in Figure 5 left), deviates from a sagittal plane, apex corneae will still be projected against the same point on the scale. The condition of this phenomenon is that the

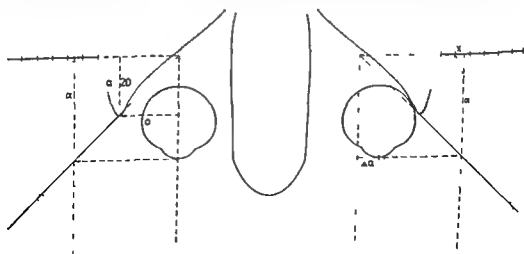


Fig 5
Geometry of the Hertel exophthalmometer

distance between the plane of the scale and the lateral orbital margin is the same as the distance between apex corneae and a sagittal plane through lateral orbital margin Hertel found this last distance to be average 20 mm and constructed his exophthalmometer according to this

For practical reasons he later rejected this construction The scale was now placed laterally on the exophthalmometer and by the help of a mirror optically transferred to the original position (Figure 1)

A parallax error may be introduced also in this instrument if the distance between apex corneae and a sagittal plane through lateral orbital margin differs from 20 mm Figure 5, right side, demonstrates this The error x may be calculated from the equation $x = \Delta a \operatorname{tg} \alpha$ Table 3 gives the size of the error for some values of Δa and α

Table 3

α	Δa	$\pm 3\text{mm}$	$\pm 6\text{mm}$
± 5		$\pm 0.26\text{mm}$	$\pm 0.53\text{mm}$
± 10		$\pm 0.53\text{mm}$	$\pm 1.06\text{mm}$

1 new exophthalmometer

On the basis of the above analysis, a new exophthalmometer has been constructed in which the sources of error mentioned have been reduced or eliminated The new exophthalmometer is of the Hertel type, that is the footplates of the instrument and the scales, are placed on both sides at the same time

Emphasis have been laid on the design of the instrument's footplate, which is straight not curved and parallel to a frontal plane (Figure 6)

Cornea is seen in profile through a right angled 45° prism The parallax problem is solved by drawing a vertical line on the frontal and the sagittal plane of the prism These lines are placed so that when the lines coincide the sight line is parallel respectively at a right angle to a frontal plane (Figures 6 and 7 left side)

By the help of a screw the prism can be moved along the arm of the exophthalmometer The prism is set in a position where the two vertical coinciding lines of the prism are seen as a tangent to cornea at apex The exophthalmometric value is now given by the position of the vertical line on the sagittal plane of prism along a scale on the arm of the exophthalmometer By a suitable design this position can be read with a high degree of accuracy

By this construction the parallax error is in principle eliminated It is taken as important that the measurement takes place in two steps First, the instrument is set and afterwards read By this procedure bias is more

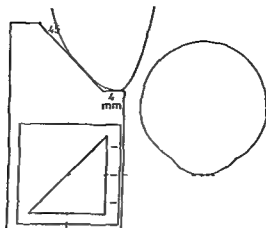


Fig 6

Detail from the new exophthalmometer. The footplate, the prism, the prism slide and the scale is seen.

or less eliminated, the first measurement does not influence the following, and several independent measurements may be performed. Thereby the error may be reduced, and an impression of the accuracy is obtained.

By an addition to the instrument the position of the eye along a vertical and a lateral co-ordinate can be measured. The reference point on the cranium is the same as in exophthalmometry, and the reference point on the eye is the centre of the pupil. A transparent Perspex plate, 8 mm thick, (Figure 7, right side) can be moved by the help of a screw at a right angle to the arm of the exophthalmometer, that is, along a frontal plane. Two

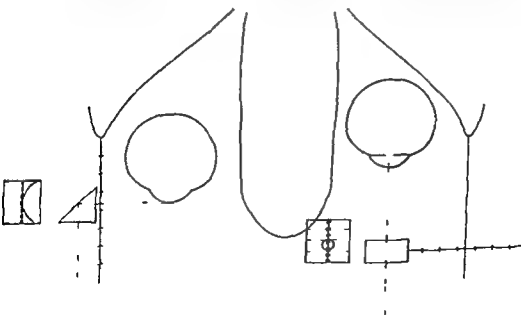


Fig 7

Geometry of the new exophthalmometer.

vertical lines are drawn, one on each side of the Perspex plate. The parallax error is eliminated when the two vertical lines coincide. The Perspex plate is set in a position where the two coinciding lines are projected against the centre of the pupil. The position of the plate is read on a scale on the instrument's arm. The reading indicates the distance between the pupillary centre and a sagittal plane through the lateral orbital margin.

The vertical co-ordinate is measured on a scale drawn on both sides of the Perspex plate after the same method as in Luedde's ruler.

With this instrument the standard error for exophthalmometry has been found to be $1/3$ mm which means that $2/3$ of the single measurements lies in the range between the average $\pm 1/3$ mm.

Exophthalmometry has commonly been regarded as an examination with limited value. In my opinion this is caused by inaccurate instruments; thus the results have not been sufficiently reproducible. Measurements with a more accurate exophthalmometer are valuable, especially in comparative exophthalmometry.

Summary

Absolute, comparative and relative exophthalmometry is defined. The concept of reference points is emphasized. The exophthalmometric value is defined as the distance from apex corneae to a frontal plane through the deepest point on the lateral orbital margin. Technical problems in exophthalmometry are considered under the following headings: 1. The position of the zero point. 2. The direction of the scale. 3. The parallax error.

A new exophthalmometer is described.

REFERENCES

- Cohn H. Jahresber d. Schles. Ges. f. Naturh. 1865 43 156.
Cohn H. Messungen der Prominenz der Augen mittels eines neuen Instrumentes des Exophthalmometers. Klin. Monatsbl. f. Augenh. 1867 5 339.
Deus L. C. Exophthalmometry. Amer. J. Ophth. 1957 43 37.
Hertel E. Ein einfaches Exophthalmometer. Arch. f. Ophth. 1905 60 171.
Luedde W. H. An improved transparent exophthalmometer. Amer. J. Ophth. 1938 21 476.

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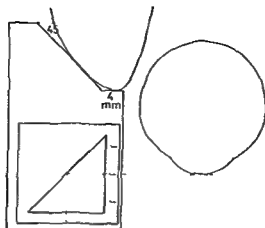


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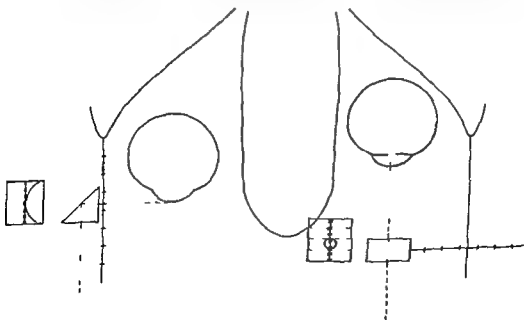


Fig 7

Geometry of the new exophthalmometer

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REFERENCES

- Cohn H. Jahresber. d. Schles. Ges. f. Naturh. 1865 43 1-6
Cohn H. Messungen der Prominenz der Augen mittels eines neuen Instrumentes des Exophthalmometers. Klin. Monatsbl. f. Augenh. 1867 5 339
Deus L. C. Exophthalmometry. Amer. J. Ophth. 1957 43 37
Hertel E. Ein einfaches Exophthalmometer. Arch. f. Ophth. 1905 60 171
Luedde H. An improved transparent exophthalmometer. Amer. J. Ophth. 1938 21 476

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LONG-TERM PROGNOSIS IN MALIGNANT EXOPHTHALMOS

By

Ruth Riise

The term malignant exophthalmos embodies the eye symptoms occasionally encountered in thyro hypophyseal disease exophthalmos, disturbances of motility, oedema, stasis, optic nerve involvement and corneal ulceration because of exposure, in rare cases complicated by panophthalmia and destruction of the eyes

The disease may also be called endocrine exophthalmos, endocrine ophthalmopathy, progressive exophthalmos, thyrotropic exophthalmos and thyro hypophyseal syndrome

It is a fairly infrequent disease, usually appearing in the euthyroid patient

Numerous experimental studies have contributed to the elucidation of the pathogenesis (*Horster, Tengroth*) which, however, still remains to be fully clarified

In 1954, *Dobyns* and *Wilson* showed that serum from patients with malignant exophthalmos contains an exophthalmos producing substance formed in the pituitary body, but not identical with thyrotrophin

Furthermore the long acting thyroid stimulator (LATS) exerts an influence. It is formed outside the pituitary body and is believed to possess autoimmune properties (*Werner*)

A mucinous oedema is formed in the orbital tissue and in the muscles of the eye (*Wegehus, Asboe Hansen and Lamberg*), and an accumulation of mucopolysaccharides in the skeletal muscles occurs (*Asboe Hansen, Iversen and Wichmann*). Increased content in the orbital tissue of glucoproteins has also been demonstrated (*Præme*)

The numerous suggestions for therapeutic measures available, bear witness to therapeutic difficulties in connection with malignant exophthalmos

General systemic treatment with glucocorticoids causes a regression of the oedema of the orbital tissue and affects an autoimmune process, if

any Favourable results of this treatment have often been seen (*Werner, Lamberg Horster, Macoul and Dellaparte, Bonnyns et al Lipman et al*), but some workers doubt the advisability of corticoid treatment, it having been shown that corticoids can aggravate experimental exophthalmos produced by thyrotropin (*Brain*) Furthermore, exophthalmos has developed occasionally in patients after treatment with corticoids for other diseases (*Slansky et al*)

Thyroid extract has been used very extensively (*Brain, Horster*) During recent years favourable results have been reported after treatment with the synthetic D thyroxin (*Horster, Tengroth, Vesterdal*) However, it appears that D thyroxin has not been sufficiently effective in the most severe cases of malignant exophthalmos (*Horster, Green and Farren*)

Treatment with oestrogens has been attempted but with doubtful effect (*V A Jensen Lederer*)

By retrobulbar X ray treatment and retrobulbar injection of steroids or hyaluronidasis, transient and partial remission of the oedema may be obtained (*Horster Kadin Roelsen and Skjærbæk Olesen*)

Formerly surgical orbital decompression was a method of treatment frequently suggested (*Naffziger Lyle*) but has now been replaced by medical therapeutics In cases of complications threatening the visual acuity orbital decompression may however still be employed (*Backlund*)

Tarsorrhaphy may be sufficient (*Ehlers*)

Many workers consider malignant exophthalmos to be a self limited disease and this can complicate an evaluation of the effect of treatment However only few studies are available in which patients have been observed over appreciable periods of time Of 24 patients who had been followed for many years *Brain* found 3 cured 10 improved and 11 unchanged Similar results were found by *Bardram* who collected 24 cases with an average observation period of three and a half years from the literature

Own material

With the object of elucidating the long term prognosis in malignant exophthalmos a follow up study was carried out of some of the patients who during the period from 1953 to 1963 were checked in the Eye Clinic at the Copenhagen Municipal Hospital

Only severe cases were included

By this procedure the number was limited to 16 3 of those had died and 3 did not appear for examination

Hence the material comprises 10 patients with severe malignant

exophthalmos who were examined after periods of from 5 to 15 years. They were 5 females and 5 males, aged 47-77 years.

Nine patients were euthyroid at the initial examination. One patient presented slightly elevated BMR.

In 5 of the patients the eye symptoms appeared after thyroidectomy, in one the disease presented itself in connection with the menopause and in the remaining 4 patients, all males, the disorder set in spontaneously.

The diagnosis was established by relating the clinical findings to the results of the laboratory investigations (BMR, serum cholesterol, PBI, T_3 test), X ray examination (orbita, arteriography) and histological examination of skeletal muscles.

Table 1

	Visual acuity		Optic atrophy		Venous congestion		Oedema	
	I	II	I	II	I	II	I	II
1	6/12 — 6/60	6/9 — 6/9	—	—	+	—	+	+
2	6/36 — 6/6	6/9 — 6/9	+	+	+	+	—	+
3	6/6 — 6/6	6/6 — 6/6	—	—	+	—	+	+
4	6/6 — 6/6	6/6 — 6/6	—	—	—	—	—	—
5	6/6 — 6/24	6/6 — 6/60	—	—	+	+	+	+
6	6/6 — 6/12	6/6 — 6/6	—	—	—	+	—	—
7	6/24 — 6/18	6/18 — 6/9	+	+	+	—	—	+
8	6/6 — 6/6	6/6 — 6/6	—	—	—	—	—	—
9	6/6 — 6/6	6/6 — 6/6	—	—	+	—	+	—
10	6/6 — 6/6	6/60 — 6/9	—	—	—	—	+	—

During the initial examination, deterioration of visual acuity was found in 5 patients. In No. 5, the deterioration of visual acuity in the left eye, however, was the result of squint amblyopia. In the remaining patients, the deterioration must be regarded as being associated with the current disease. All these patients showed improvement of visual acuity at the follow up examination. In No. 10 the follow up examination revealed senile degeneration of the macula.

Two patients presented optic atrophy both at the initial and at the check up examination. In both cases the atrophy was unilateral. None presented papilloedema.

Stasis of the fundus veins and the episcleral vessels diminished during the follow up period. The oedema of the eye surroundings and the conjunctiva was still present, but no tension of the tissue was observed.

Visual field defects were observed initially in two cases (Nos. 1 and 2). In both patients the visual field was found to be normal at the follow up.

At this time No 7 had developed visual field defect. The appearance of the defects varied, from one large defect in both lower quadrants to partial lower temporal quadrant anopsia and bitemporal defect. In one case the defect resembled a Bjerrum scotoma. Similar defects have been demonstrated by *Hedges and Shee* and *Day and Carroll*. This is suggestive because *Pohjanpelto* has shown that the intraocular tension in these patients is higher than that found in a normal material.

Table 2

Exophthalmometry		Diplopia		Limitation of movement		Therapy
I	II	I	I	I	II	
1 26-24	20-20	+	+	+	+	D Thyroxin Hyaluronidase retrobulb
2 28-26	27-25	-	-	+	+	Corticosteroids Tarsorrhaphia Ismelin
3 30-27	23-21	+	+	+	+	Thyroid extract Corticosteroids
4 21-18	18-17	+	+	+	-	
5 25-19	24-22	-	-	-	+	
6 18-25	25-25	+	+	+	+	Corticosteroids Tarsorrhaphia
7 20-18	32-29	-	-	-	-	Tarsorrhaphia
8 22-18	21-18	+	-	+	+	
9 30-26	normal (un measured)	+	-	+	-	Corticosteroids Thyroid extract
10 22-22	20-19	+	+	+	+	ACTH Corticosteroids Thyroid extract

At the follow up study exophthalmos persisted in most of the patients. In Nos 4 and 9 the exophthalmos had disappeared (No 9 refused measurement). No 6 was found to have developed bilateral exophthalmos.

Diplopia in the primary position and limitation of motility were frequent findings also at the follow up. Elevation and abduction were most often affected.

At the initial examination, patient No 7 had a keratitis which healed during the follow up period.

The therapeutic efforts have been multiple. Thyroid extract, D thyroxin, glucocorticoids, retrobulbar injection of hyaluronidase and tarsorrhaphia have been employed.

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4	6/6 — 6/6	6/6 — 6/6	—	—	—	—	—	—
5	6/6 — 6/24	6/6 — 6/60	—	—	+	+	+	+
6	6/6 — 6/12	6/6 — 6/6	—	—	—	+	—	—
7	6/24 — 6/18	6/18 — 6/9	+	+	+	—	—	+
8	6/6 — 6/6	6/6 — 6/6	—	—	—	—	—	—
9	6/6 — 6/6	6/6 — 6/6	—	—	+	—	+	—
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- Day R and Carroll F Arch Ophth 67 289 (1962)
 Day R and Carroll F Arch Ophth 79 279 (1968)
 Dobyns H M and Wilson L A J Clin Endocr 14 1393 (1954)
 Ehlers H Ugeskr Læg 130 728 (1968)
 Greene R and Farran H E Brit Med J 2 1027 (1958)
 Hedges T and Schae H Arch Ophth 54 885 (1955)
 Horster F A Endocrine Ophthalmopathy Springer 1967
 Jensen V A Acta Ophth 18, 1 (1940)
 Kadin M Am J Ophth 33 962 (1950)
 Lambert B A Acta Med Scand 156 391 (1957)
 Lederer J Ann Oculist 181 37 (1948)
 Lipman L M Green D E Snyder V J Nelson J C and Solomon D H Am J Med 43 486 (1967)
 Lyle T A Trans Ophth Soc U K 80 107 (1960)
 Macoul A L and DellaPorta A Brit J Ophth 53 203 (1969)
 Medin M M Am J Ophth 34 1587 (1951)
 Naffziger H C Am J Surg 75 25 (1948)
 Pohjarpelto P Acta Ophth suppl 97 (1968)
 Pransky G Exptl Eye Res 8 21 (1969)
 Roelun E and Skjærbæk Olesen Ugeskr Læg 1 13 (1968)
 Slansky and al Arch Ophth 77 579 (1967)
 Tengroth B Acta Ophth Suppl 65 (1961)
 Tengroth B Acta Ophth 42 859 (1964)
 Tengroth B and Frien L in Asboe Hansen Hormones and Connective Tissue Munksgaard, Copenhagen 1966
 Tøsterdal E Acta Ophth 43 587 (1965)
 Wegelius O Asboe Hansen G and Lambert B A Acta Endocrin 25 452 (1957)
 Werner S C in Thyrotoxicosis (Proc of symp Edinburgh) 1967

Discussion

E Tøsterdal (Copenhagen)

To Dr Ruse's paper on the long term prognosis of malignant exophthalmos I should like to add a few remarks and submit a short survey on the symptoms, signs and therapeutic results in a material from the Finsen Institute Copenhagen from the period 1949-1969. Since in this hospital the isotope department, the surgical department and the department of general medicine have taken particular interest in thyroid diseases numerous patients are being referred to us especially patients who have been unsuccessfully treated elsewhere. I shall not deal with the ordinary — I might say uncomplicated — exophthalmos but only with cases that may be designated as post thyrotoxic exophthalmos or malignant exophthalmos for which Dr Ruse employs the following diagnostic criteria.

Palpebral and orbital oedema, exophthalmos, episcleral venous congestion and in more serious cases chemosis, disturbances of motility with pareses of the ocular muscles due to infiltration in and around the muscle fibres, and lastly a closure defect resulting in keratitis etc. No mention will be made of the various theories concerning a pituitary thyroid imbalance, EPS, LATS etc.

During the named 10-year period an ophthalmological diagnosis of this disease was made in 51 persons. But 6 have to be excluded from the material because they were not treated (either because they died or were discharged to distant parts of Denmark).

Conclusion

The course of disease was roughly identical in the 10 patients followed up

The results of the follow up study give rise to the following comments

During the stage of culmination, malignant exophthalmos causes much discomfort and anxiety to the patient and requires treatment. Consequently, only few patients have not been treated, employing two or more of the measures described in the foregoing

However, we can only suppose that the disease is self limited, with a protracted course lasting for months or years. An ascending phase is succeeded by culmination at individually varying stages, characterized by stasis and tissue infiltration which seems to incarcerate the bulbus. Then follows a descending phase, with a diminishing of the congestion and gradual normalization of the density of the periorcular tissue, accompanied by a feeling of improvement being experienced by the patient.

The exophthalmos persists and, of course, it will give rise to cosmetic problems, whereas the disturbances of motility will also persist and will cause much complaint on rare occasions only.

Only palliative treatment can be offered. Critical phases will, presumably, best be alleviated by means of short term intensive steroid treatment (e.g., 150 mg prednisone daily).

It is extremely important to explain, in comforting terms, the normal course of the disease to the patient.

Summary

The long term prognosis in malignant exophthalmos is elucidated by a follow up study after 5-15 years in 10 patients with severe symptoms.

It is concluded that the disease is self limited. After periods of months or years, some remission may occur, followed by a stationary stage, characterized by exophthalmos and disturbances of motility.

During critical phases, brief treatment with large doses of steroids is recommended.

REFERENCES

- Asboe Hansen, G. Jørgensen & Wichmann. *Acta Endocrin* 11: 376 (1952)
Backlund E. O. *Acta Ophth* 46: 35 (1968)
Bardram M. T. *Acta Ophth* 22: 1 (1944)
Bonnyns, M. Demester, Markine N. Calay R. and Bastenne P. 1. *Acta Endocrin* 58: 581 (1968)
Brain, R. *Trans Ophth Soc U.K.* 57: 107 (1937)
Brain R. *Lancet* 1, 109 (1959)

The follow up periods range from 9 months to 9 years averaging $4\frac{1}{2}$ years. All the patients were examined by me in the spring of 1969

In 19 cases the treatment was discontinued more than 6 months ago without there having been any recurrences. The others are still being treated.

Table 3 shows that disturbances of motility with diplopia were found in 27 out of the 45 patients i.e. in 60%. As may be seen this did not occur among the patients treated with ^{131}I iodide. In 23 the motility had returned to normal at the time of the follow up examination while in 4 there has been no remission. Out of the latter patients 3 have been treated for less than a year.

Table 3
Restriction of motility with diplopia

	Before treatm	After treatm
Group I (18)	11	2
Group II (12)	8	2
Group III (6)	0	0
Group IV (9)	8	0
45	27	4

Closure defects of the lids were found in 18 patients when first seen. 3 of them had keratitis which was cured. One who was treated before Ismelin was available developed a corneal macula with impaired vision (6/24) in one eye.

One patient had a choked disc but this soon subsided without any secondary atrophy. Tonometry was performed in all cases, but without disclosing glaucoma.

The treatment was exclusively medical including local eye drops and ointments.

Depending upon the level of metabolism the following treatment schedule was used.

Table 4
Treatment of malignant exophthalmos

	^{131}I possibly combined with non radioiodide
1 Still hyperthyroid pts.	+ D-thyroxine + Ismelin eyedrops
2 Euthyroid pts.	D-thyroxine + Ismelin eyedrops
3 Hypothyroid pts	L-thyroxine + D-thyroxine + Ismelin eyedrops

In addition 3 cases of severe keratitis with exophthalmometric readings (Hertel) exceeding 30mm received glucocorticoids and corticotrophin in high doses concurrently with the other medication.

The remaining 45 patients, 40 women and 5 men, were divided into 4 groups (Table 1)

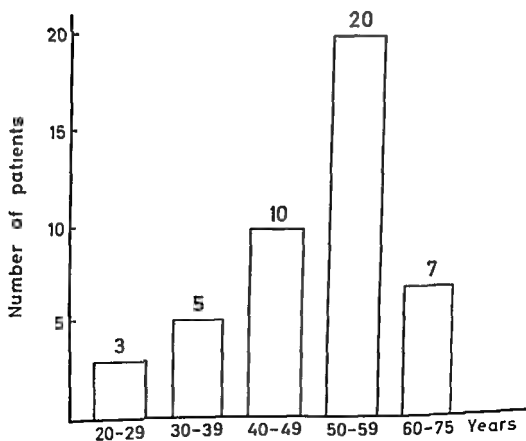
Table 1
Case material

Endocrine exophthalmos (malignant) arising after		No. of pts.
Group		
I	Thyrotoxicosis treated by thyroidectomy	18
II	Thyrotoxicosis treated by synthetic antithyroid drugs	12
III	Thyrotoxicosis treated by ^{131}I and de	6
IV	No history of thyroid disease	9
Total		45

36 had a history of thyrotoxicosis and the exophthalmos had not developed until anti thyrotoxic therapy had been instituted. In 9 cases there was no history of thyroid disease.

Table II gives the age distribution. The majority were between 40 and 60 years of age. Only 7 of the women had not entered the menopause at the onset of the disease.

Table 2
**AGE DISTRIBUTION IN PATIENTS
WITH MALIGNANT EXOPHTHALMOS**



The follow up periods range from 9 months to 9 years averaging $4\frac{1}{2}$ years. All the patients were examined by me in the spring of 1969.

In 19 cases the treatment was discontinued more than 6 months ago without there having been any recurrences. The others are still being treated.

Table 3 shows that disturbances of motility with diplopia were found in 27 out of the 45 patients i.e. in 60%. As may be seen this did not occur among the patients treated with ^{131}I iodide. In 23 the motility had returned to normal at the time of the follow up examination while in 4 there has been no remission. Out of the latter patients 3 have been treated for less than a year.

Table 3
Restriction of motility with diplopia

	Before treatm	After treatm
Group I (18)	11	2
Group II (12)	8	2
Group III (6)	0	0
Group IV (9)	8	0
45	27	4

Closure defects of the lids were found in III patients when first seen. 3 of them had keratitis which was cured. One who was treated before Ismelin was available developed a corneal macula with impaired vision (6/24) in one eye.

One patient had a choked disc but this soon subsided without any secondary atrophy. Tonometry was performed in all cases but without disclosing glaucoma.

The treatment was exclusively medical including local eye drops and ointments. Depending upon the level of metabolism the following treatment schedule was used.

Table 4
Treatment of malignant exophthalmos

	^{131}I possibly combined with non radioiodide
1 Still hyperthyroid pts	+ D-thyroxine + Ismelin eyedrops
	D-thyroxine
2 Euthyroid pts	+ Ismelin eyedrops
	L-thyroxine
3 Hypothyroid pts	+ D-thyroxine + Ismelin eyedrops

In addition 3 cases of severe keratitis with exophthalmometric readings (Hertel) exceeding 30mm received glucocorticoids and corticotrophin in high doses concurrently with the other medication.

In two cases lower doses of steroids were administered because of co existing diseases but this proved to aggravate the orbital tension

As already mentioned, no form of surgery was used, neither operations to relieve orbital tension, tarsorrhaphy, nor operations on the ocular muscles

After the advent of Ismelin eye drops, a 5% guanethidine solution from Ciba, we have had no problems on account of lagophthalmos and closure defects. The exophthalmos persisted in most cases, but in practically all considerably diminished, depending upon how early the treatment was instituted. The average diminution was 3mm and the result was most favourable in the predominantly unilateral types

Lagophthalmos, palpebral oedema, orbital tension, episcleral venous congestion, etc. subsided and as already mentioned motility was restored in the majority of cases

I quite agree with Dr Riise that malignant exophthalmos runs a self limiting course, so that treatment should be instituted primarily during crises to counteract complications deleterious to the eye

But I feel, also on the basis of the somewhat more optimistic results mentioned here to day, in particular concerning restoration of motility that long term therapy, especially with D thyroxine, should be given after the acute phase. The effect of D thyroxine is beyond doubt as seen initially from the increase in the exophthalmometric readings when the drug has to be discontinued for purposes of scanning

The difference between D and L thyroxine has been a matter of much discussion. We have alternated (in euthyroid subjects) but owing to unfortunate thyrotoxic episodes and cardiac complications with atrial fibrillation on L thyroxine, we returned to D thyroxine

In respect to the clinical diagnosis, let me point out the numerous apparently unilateral cases of endocrine exophthalmos which turn out to be in fact bilateral as exophthalmometric readings in the contralateral eye decrease after the treatment is instituted. Frequently, these cases pass through a cycle the contralateral eye becoming for a time the exophthalmic one. This was observed in 6 patients

In conclusion it may be said that with the therapeutic aids available at present the ophthalmologist can in close collaboration with the internists treat all cases of malignant exophthalmos without resorting to surgery with an acceptable cosmetic as well as functional result. Therefore as Dr Riise said we can console the patients by describing to them the usual course but we must emphasize to them that the treatment has to be continued for a long time

Incidentally, it will probably not be long before current experimental research into malignant exophthalmos yields results that open up a possibility of preventing this ophthalmopathy

Peep Algvere (Stockholm)

An extradural decompression operation of the orbit by resecting a large portion of the lateral wall and of the roof has been recommended as a possible way of treating progressive endocrine exophthalmus which has been resistant to other types of non surgical treatment. After the operation one has noticed an improvement of the visual acuity and satisfactory alleviation of the signs of exophthalmus (Ref Backlund E O Acta Ophth 1968 46 535)

H Ehlers (Copenhagen)

The malignant exophthalmus shows certain characteristics

- 1 Occurs in clinical euthyroid patients
- 2 Acute manifestation
- 3 It may be unilateral or it may appear at different times on the two sides

- 4 It may produce ocular complications (optic disc changes visual field defects)
- 5 The appearance of dark thick episcleral veins
- 6 The disease regresses very slowly

All these changes can hardly be explained by hormonal changes alone. One has to assume that local processes causes stasis and thrombosis. In the eye-department at Rigshospitalet Copenhagen we have treated the acute cases with local manipulation compression anticoagulation and diuretica.

T Bertelsen (Bergen)

The pressure in the orbit is normally approx 30mm H₂O and seldom rises to values higher than 60mm H₂O. In the cranial cavity the pressure is often 150mm H₂O. How can it then be possible to increase the volume of the orbit at the expense of the cranial cavity by Naftziger's operation?

From the Eye Department (Heads *B Lauetz* and *H H Seedorff*), Department of Neuroradiology (Heads *H H Jacobsen* and *J Lester*), and Department of Neurosurgery (Heads *J Riishede*, *A Vernet* and *P Rasmussen*), Rigshospitalet, Tagensvej University of Copenhagen, Denmark

OPTIC GLIOMA CLINICAL FEATURES AND TREATMENT

By

J Fog, H H Seedorff and K Vernet

Optic glioma is defined as a benign, slow growing, non metastasizing brain tumour which occurs mostly in childhood (75% before the age of 12 years) It is rare, the incidence having been stated to be 0.8% of intracranial tumours (Martin and Cushing 1923)

One of the first who tried to classify intradural tumours of the optic nerve was von Graefe (1864) Since that time a multitude of papers have been published on primary optic tumours The relationship of primary optic glioma to Recklinghausen's neurofibromatosis (1882) has also been known for almost 100 years It is worth noting that Scandinavian authors have given weighty contributions on this subject, most recently Ehlers (1966), but also Alms (1943), Brændstrup (1944), Godtfredsen (1947), Borberg (1951), and Ladekarl (1964) In his recent paper Ehlers took stock of the subject on the basis of his own studies and the literature Certain authors, *int al* Davis and Byrki, believe that primary optic glioma is only one sign of a disseminated disease and that it *may* represent the first and only sign of Recklinghausen's disease Against this view there is the failure to find histological similarities between optic glioma (arising in glial tissue) and von Recklinghausen's disease (arising in Schwann's cells) Erna Christensen and Ry Andersen (1952) tried classifying the primary cells of optic glioma, but later, like most other workers, gave up this classification Therefore, the more neutral term optic glioma must be kept up for the time being

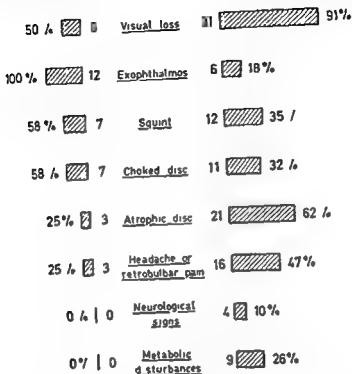
Figure 1 illustrates schematically the incidence of symptoms and signs in glioma of the optic nerve in relation to the situation of the tumour in the nerve (after Dodge, *et al* 1958)

Present Investigations

As a consequence of the borderline position of the optic nerve between ophthalmology and neurology, a combined assessment of optic glioma

Glioma restricted to
optic nerve (12 pts)

Glioma affecting optic nerve chiasm
and optic tract diffusely (34 pts)



Distribution of patients with glioma restricted to optic nerve and patients with glioma affecting the optic nerve chiasm and optic tract diffusely (46 pts)
(After Dodge et al 1958)

Fig 1

was undertaken from the point of view of the ophthalmological and neuroradiological diagnosis as well as neurosurgical treatment. The main problem must be (1) how to diagnose a tumour in the optic nerve as early as possible and (2) how to attack it surgically.

Below follow four case reports on patients with optic glioma treated in Rigshospitalet, University of Copenhagen, within the past few years.

In all four cases the clinical ophthalmological signs were unilateral exophthalmos, impaired vision, choked disc and squinting, but no neurological signs were present. Other findings and the treatment of the individual patients were as follows.

Case 1 A baby aged 5 months with café au lait spots on the skin. Orbitography showed a tumour in the optic nerve with an enlarged optic foramen (Figure 2). The operation was carried out in two stages: first



Fig 2

Case 1 Orbitography Frontal view The circular defect centrally in the contrast medium represents the greatly enlarged optic nerve

intracranial resection of the optic nerve from the foramen to the border of the chiasm, thereafter extradural intraorbital resection of the optic nerve from the globe to the optic foramen Histological diagnosis Glioma of the optic nerve removed in healthy tissue, but with intracranial invasion

Case 2 A child, aged 2½ years, with Recklinghausen's neurofibromatosis X rays showed a normal optic foramen Orbitography Retrobulbar tumour arising in the optic nerve (Figure 3) The operation was performed in two stages, first an extradural procedure on the temporal region, resecting the orbital part of the optic nerve as far as the optic foramen As signs of invasion through the foramen were found, a transcranial intradural procedure was done later, removing the grossly normal looking nerve as far as the chiasm Histological diagnosis Glioma of the optic nerve right to the last section at the chiasm border, i.e. non radical removal

Case 3 A child, aged 3½ years, with café au lait spots on the skin X rays Enormous enlargement of the optic foramen Orbitography Considerable enlargement of the optic nerve (Figure 4) An intracranial, exploratory operation revealed fusiform swelling of the nerve, with in

vasion of the chiasm and optic tract Histological diagnosis Glioma tissue in the optic nerve Treated by X radiation

Case 4 A child aged 4 years without any signs of Recklinghausen's disease X rays Considerably enlarged optic foramen Orbitography Enormous tumour in the optic nerve (Figure 5 and 6) A transcranial exploratory operation revealed fusiform swelling of nerves with invasion of the chiasm Radical removal was out of the question, and the patient was transferred for X ray therapy

Diagnosis

The four case histories represent even transitions from a tumour restricted to the optic nerve to massive invasion of glioma tissue into the chiasm and optic tract A correct and sufficiently early diagnosis must be based upon the ophthalmological signs (unilateral axial protrusion and choked disc or atrophy) as well as the radiological findings Visual field



Fig 3

Case 2 Orbitography Lateral view The contrast medium has been injected partially subdurally outlining the expanded optic nerve in the posterior part of the orbit. Escape of contrast medium above the sella turcica and on the clivus



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Fig 5

Case 4 Orbitography Frontal view Enormous tumour of the optic nerve The contrast medium surrounds the tumour inside the dural sheath

vein is devoid of risk and well suited for diagnosing retrobulbar tumours but not dependable enough for recognizing tumours of the optic nerve. The most important X-ray method for this purpose is orbitography. At Rigshospitalet, University of Copenhagen, this study has been done with water soluble contrast medium for the past 6 or 7 years. During this period we have carried out 50 studies, finding tumours of the optic nerve in 6, including the 4 patients described above. We prefer orbitography by positive contrast medium to pneumo-orbitography because *In the first place* this affords films of great diagnostic value, giving information about expansive lesions, both within and outside the muscle cone with good visualization of the optic nerve. *Secondly*, tomography is unnecessary and the projections are simple. *Thirdly*, orbitography by positive contrast is not much of a strain on the patients and may be accomplished within 30 minutes. We have not observed serious complications apart from one case of transient visual impairment.

Pneumo-orbitography, as described by Bertelsen (1966), among others, carries in our opinion a certain risk. Unlike orbitography using positive contrast medium, it presupposes tomography in 2 planes, and the films



Fig 4

Case 3 Orbitography Optic foramen projection The contrast medium has spread inside the muscle cone The tumour of the optic nerve presents itself as a clear cut defect in the contrast partially overlapping the greatly expanded optic foramen

examination was out of the question, as the patients were too young The radiography may be done by 3 methods

- 1 General view of the orbit including projections to visualize the optic foramen
- 2 Orbital venography and arteriography
- 3 Orbitography using air or water soluble contrast media

A general view of the orbit shows signs of abnormalities in only about 20% of the cases having unilateral exophthalmos Furthermore, the optic foramen is subject to certain anatomical variations, so that an increase of 20% or more in its diameter, as compared with the unaffected side, must be demanded if the appearances are to be interpreted as abnormal, cf Goalwin's (1927) study of 1,000 normal optic foramina only 55% of which were symmetrical Three of our patients had enlargement of the optic foramen according to these criteria Therefore, general views of the orbit are unsatisfactory and carry too much uncertainty to be the only X ray procedure

Orbital venography, performed percutaneously through the frontal

approach it is possible to inspect only the anterior part of the orbit, it hardly ever permits radical excision of retrobulbar tumours, and gives no access to the region of the optic foramen. And by this route it is of course, impossible to reach an intracranial extension of an optic glioma.

Cushing and Dandy, around 1920 developed the transfrontal approach to the orbit by extradural removal of the orbital roof and the lateral orbital wall. This affords a far better view of the orbit, right back to the optic foramen. At the same time it is possible to explore the intracanalicular and intracranial part of the optic nerve and chiasm. This is of particular importance in optic gliomas where there is no definite possibility of deciding preoperatively whether the tumour is extending through the optic foramen. As already mentioned, X-ray examination of the optic foramen gives no definite guidance in this respect. In one of our patients (Case 2) the optic foramina were normal and equal, and the optic nerve was grossly normal in its intracranial course. However, microscopic examination showed tumour cells in the removed optic nerve right to the point of resection at the chiasm. In another patient (Case 1) one optic foramen was 5 mm in diameter the other one 7 mm. In this case the tumour had spread to the optic canal, but the site of resection at the chiasm showed no signs of neoplastic infiltration.

The only means of preventing a glioma in one optic nerve from spreading to the chiasm and thence further is by cutting the optic nerve at the angle of the chiasm (or more correctly 1-2 mm anterior to it). In our opinion therefore this should be done primarily in all cases of optic glioma showing an enlarged optic foramen. In other words, these growths should always be approached by the transfrontal route. The same applies of course to patients in whom the clinical findings indicate that the tumour has spread to the chiasm or hypothalamus. In such cases the problem is a different one. Generally there is only a question of exploration and removal of a biopsy in order to decide on the indications for X-ray therapy. A shunt operation may be considered, if there is a risk of the tumour blocking the foramen of Monro.

But in patients without enlargement of the optic foramen and without any clinical evidence of an optic glioma or perhaps even evidence of a tumour situated outside the optic nerve there is a lateral extracranial approach which permits a far better exposure of the orbit and the orbital contents than the classical Kronlein operation.

This operation appears to have been described first by Welti in Paris in 1943 but it was developed in several centres independently, as a decompression procedure in malignant exophthalmos. It represents the inferior part of the transfrontal operation.

From an initial burr hole just behind the zygomatic process of the



Fig 6

Orbitography Lateral view of the same patient as in Fig 5 The tumour is almost spherical The contrast medium in the subdural space is spreading above the sella turcica

are not at all easy to read Moreover, we do not know its diagnostic accuracy

In orbitography with positive contrast medium the diagnostic accuracy has been found to be 80% (Lombardi and Palcerini)

Our orbitographies were performed in the Department of Neuro radiology by experienced radiologists who use the same technique of injecting the contrast medium as in ordinary retrobulbar anaesthesia The situation of the tip of the needle is checked by control films, and thereafter 3-4 ml of a mixture of lidocaine 2% and Urografin 45% is injected Exposures are made immediately in the a-p, lateral, and p-a views The series is repeated at the end of 10 min to show a possibly better distribution of the contrast medium At the end of 20 min the contrast medium has been eliminated This procedure does not give rise to more discomfort than does ordinary retrobulbar anaesthesia

Treatment

The resection of the lateral margin and the anterior part of the lateral orbital wall introduced by Kronlein in 1888, was for many years the classical and only approach to the orbit Through this very limited

approach it is possible to inspect only the anterior part of the orbit, it hardly ever permits radical excision of *retrobulbar tumours*, and gives no access to the region of the optic foramen. And by this route it is of course, impossible to reach an intracranial extension of an optic glioma.

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Discussion

O. A. Jensen (Copenhagen)

It is our experience that gliomas of the optic nerve tend to grow backwards in spite of the limitations of the bony channel. In view of this we strongly endorse Dr. Seedorff's statement that all methods of examination must be employed in order to clarify the diagnosis as soon as possible. If clinical methods have no result an explorative orbitotomy must be performed. Otherwise many of these cases very soon become inoperable.

frontal bone, the orbit may be opened. From this site, the lateral wall may be removed by a rongeur down to the superior orbital fissure, and practically the entire orbit, including the optic canal, if desired, may be unroofed. This affords free access to the entire contents of the muscle cone including the optic nerve. If necessary, its intracranial part may be explored also in this or a later stage.

This entire subject has been reviewed by Zander and Campiche (1966).
Summary

Orbital tumours, including optic gliomas, make up a typical border line subject between two disciplines in which neurosurgical technique has created a possibility for considerably better and more effective approaches. However, the most favourable results are obtained by collaboration between neuro radiologist, neurosurgeon, and ophthalmologist, and an experienced ophthalmic pathologist may prove of invaluable aid, not least in planning possible secondary procedures.

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REFERENCES

- Alm J. *Nord Med* 1943, 18: 897.
 Bertelsen T. I. *Acta Ophthalm* 1966 151: 309.
 Borberg A. Clinical and genetic investigations into tuberous sclerosis and Recklinghausen's neurofibromatosis. Thesis Kobenhavn 1951.
 Brøndstrup P. *Acta Ophthalm* 1944 22: 72.
 E. Christensen and S. Ry Andersen. *Acta Psychiatr scand* 1952 27: 5.
 Cowie J. W. and J. S. Groves. *Brit J Ophthalm* 1955 39: 283.
 Dodge W. H., Love Craig J. G. W., Docherty W. M., Keams M. B. and Holman P. *Arch Neurol Psychiat* 1958 79: 607.
 Ehlers H. *Acta Ophthalm* 1966 151: 284.
 Godfredsen, E. *Acta Ophthalm* 1947 25: 279.
 von Graefe A. *Arch f Ophthalm* 1864 10: 193.
 Goalluin, H. A. *JAMA* 1927 89: 1745.
 Ladekarl, S. *Acta Ophthalm* 1964 2: 42.
 Lombardi, G. *Acta Radiol* 1957 47: 417.
ibid *Radiology in neuro ophthalmology* Williams & Wilkins Baltimore 1967.
ibid *Arch of Ophthalm* 1967 78: 306.
 Martin, P. and Cushing, H. W. *Arch of Ophthalm* 1923 52: 209.
 von Recklinghausen F. Über die multiplen Fibrome der Haut und ihre Beziehung zu den multiplen Neuronen. Berlin A. Hirschwald 1882.
 Zander, E. and Campiche R. *Confin Neurol* 1966 28: 208.

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From the Ophthalmic Pathology Laboratory, University of Copenhagen
Head *S Ry Andersen*

MUCOSUBSTANCES OF MIXED LACRIMAL GLAND TUMOURS

Histochemical and histogenetic aspects

By

O A Jensen

BRIEF REPORT

(The full report has been published in *Acta path microbiol scand* Section A 78 110, 1970)

An earlier histochemical and biochemical examination of the mucosubstances (MS) of normal human lacrimal glands (¹) showed an abundance of sialic acid containing MS, but no sulphated MS

The purpose of the present investigation was to apply a battery of histochemical methods to sections of mixed lacrimal gland tumours to determine the pattern of MS and on the basis of the findings to consider the histogenesis

A survey of the *material and methods* may be seen in Table 1

Table 1			
<i>Material and Methods</i>			
	M	F	Total Number
1942-1967	5	5	10
Age	40-59	13-71	
Recurrences	1	1+2	4
Total material			14 tumours
Fixation	4% buffered neutral formaldehyde/24h/4 C		
Embedding	Routine paraffin technique		
Sections	4μ		

Staining

Periodic acid — Schiff

Metachromatic methods

Alcian blue affinity at different pH and electrolyte conc

Combined staining methods (CI PAS AF AB HID AB)

Fluorescence

Simple protein stains (collagen reticulin elastic tissue)

Blocking reactions

Enzyme digestion

The results indicate the presence of the following MS, using the classification of Spicer *et al* ⁽³⁾ modified by Pearse ⁽⁴⁾

- 1 G-mucosubstance
- 2 C-mucopolysaccharide
- 3 CG-mucin N±
- 4 S-mucopolysaccharide B 2 0 T
- 5 S-mucin B 2 0

The amount and localisation of these substances vary, but the distribution in the material (Fig 1) was mainly such that neutral mucosub



G = G-mucosubstance (Neutral mucosubstances)

C = C mucopolysaccharide (Connective tissue sialomucins)

CG = CG mucin N± (Epithelial sialomucins)

SB2 = S-mucin B 2 0 (Epithelial sulphomucins)

SB2T = S mucopolysaccharide B 2 0 T (Connective tissue mucopolysaccharide)

Fig 1

Localisation of the mucosubstances revealed by the histochemical methods.
Dots Epithelial strands Grey areas and stippling Interstitial substance

From the Ophthalmic Pathology Laboratory, University of Copenhagen
Head S Ry Andersen

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From the Ophthalmic Pathology Laboratory University of Copenhagen
Head S Ry Andersen

PRIMARY, HISTOLOGICALLY CONFIRMED ORBITAL
TUMOURS IN DENMARK 1943-1962
HISTOPATHOLOGICAL AND PROGNOSTIC STUDIES

By
Poul Eldrup Jørgensen

Read in an abbreviated form to the 19th Meeting of Scandinavian Ophthalmologists, Bergen 18th-21st June, 1969

Aided by a grant from the Danish Anti Cancer League

The present study consisted in an analysis and histopathological classification of all primary, histologically confirmed orbital tumours in Denmark from 1943-1962 inclusive. This 20 year period was selected as it starts at the time that the card index of the Ophthalmic Pathology Laboratory was established and the year after all malignant tumours in Denmark became notifiable to the Cancer Registry. The minimum follow up period = 5 years.

Although orbital tumours are fairly rare and the material therefore of modest size I preferred including only histologically confirmed tumours. Clinically it is seldom possible to determine the nature of the tumour. Therefore all orbital tumours should be studied histologically.

These tumours also give rise to differential diagnostic problems, especially in the presence of thyrotoxicosis but mucocoeles, metastases, tumours from adjacent structure, haematomas, thromboses in the sinus cavernosus and orbital inflammations may be confused with true primary orbital tumours.

Tumours of the orbit are situated behind the orbital septum and in or within the bony frame of the orbit. The distinction from palpebral tumours at the orbital septum is rather arbitrary. Therefore some tumours have to be designated as orbito palpebral. Such tumours were not included in the present material.

Material

The material was collected by perusing the files or case records of large and moderately large eye departments, radium centres and neuro-surgical departments. Inquiries were made in smaller eye departments.

A total of 263 patients are included in the material, which gives an incidence of 0.006% in a population of 4.332 millions.

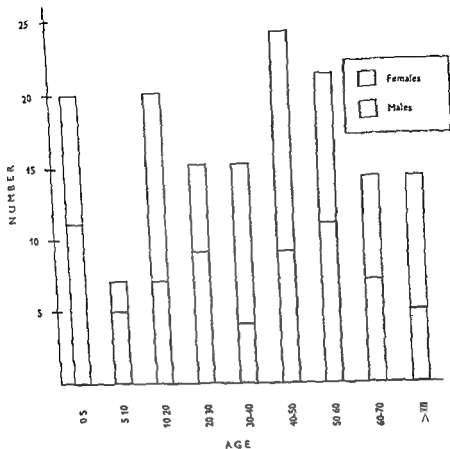
stances (G-mucin) and epithelial sialomucin (CG-mucin N_{\pm}) were found in the epithelial areas, in the vicinity of these and in the ducts, while connective tissue sialomucins (C-mucopolysaccharide) and hyaluronidase labile connective tissue mucopolysaccharide (S-mucopolysaccharide B 20 T) were found interstitially, the latter mainly centrally in the interstitia. The epithelial sulphomucins (S-mucin B 20), probably derived from the epithelium, were found in the interstitia near the epithelium.

This investigation indicates a content of two principally different types of MS in mixed tumours of the lacrimal gland: one typical of epithelial MS and the other of connective tissue MS.

This finding supports an epithelial and a mesenchymal origin. Histologically one cannot exclude the possibility that the neoplastic epithelium in one way or another can stimulate the normal connective tissue stroma such as to proliferate and produce changes in it. There is, however, no evidence of this. On the contrary, animal experiments have shown that induction of mixed tumours of the salivary gland by polyoma virus is dependent upon the presence of both epithelium and connective tissue in the gland (⁵).

REFERENCES

- 1 Jensen O A, Falbe Hansen I, Jacobsen, Toie and Michelsen, Annette. Mucosubstances of the acini of the human lacrimal gland (orbital part) I. Histochemical identification. *Acta ophthalmol (Kbh)* 47: 605-619. 1969.
- 2 Falbe Hansen I, Jensen O A and Degen Judith, A. Mucosubstances of the acini of the human lacrimal gland (orbital part) II. Biochemical identification. *Acta ophthalmol (Kbh)* 47: 620-624. 1969.
- 3 Spicer S S, Leppi T J and Stouard P J. Suggestions for a histochemical terminology of carbohydrate rich tissue components. *J Histochem Cytochem* 13: 599-603. 1965.
- 4 Pearse A G E. *Histochemistry* Ed 3 Vol 1. J & A Churchill Ltd. London. 1968. p. 304.
- 5 Dawe C J, Morgan W D and Slatnick M S. Influence of epithelial - mesenchymal interactions on tumor induction by polyoma virus. *Int J Cancer* 1: 419-450. 1966.



Sex and age incidence

Fig. 1

During the first 10 year period 50 cases occurred, while during the latter period there were 100, or twice as many. This applies to the benign as well as to the malignant tumours. Accordingly the percental distribution of these two groups is the same.

This doubling of the incidence cannot be explained solely by the increment in the population which was only 6%. But a larger number of tumours are being removed and in particular a larger number are being sent for histological study.

Figure 1 gives the age distribution and sex ratio. There is no significant sex difference.

With the division into 10 year age groups it will be seen that the number of tumours was largest from 0 — 10 years a total of 27. The most common

The number 263 must be considered a minimum of all orbital tumours, as only the histologically confirmed and primary tumours were included. Moreover, three had to be excluded because of too poor preparations and deficient data.

The histological preparations were procured for all but ten cases for which, however, I have the original histological reports.

Frequently new sections had to be cut and special stains employed.

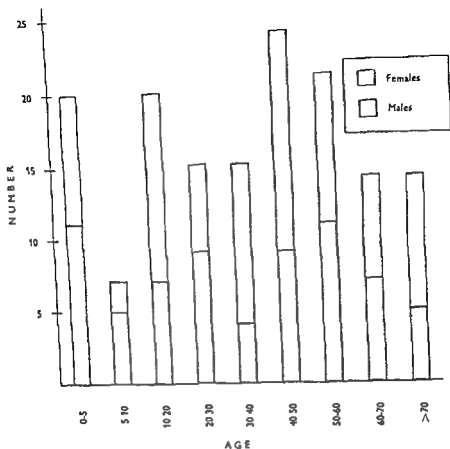
The investigation was conducted as a pilot study on 150 patients in alphabetical order.

Results

The annual distribution is shown in Table 1. On the average 7-8 cases occurred each year, the minimum being 1 in 1948 and the maximum 16 in 1957.

Table 1
Annual Distribution of Orbital Tumours

	Benign			Malignant			Total
	Male	Female	Total	Male	Female	Total	
1943	1	5	6	1	1	2	8
1944	2		2		1	1	3
1945	1	2	3		1	1	4
1946	4	2	6	1		1	7
1947	1	1	2		2	2	4
1948	1		1			0	1
1949	4	1	5	3		3	8
1950	1	2	3	1	2	3	6
1951	1	3	4	1		1	5
1952	2	1	3		1	1	4
1953	1	4	5		2	2	7
1954	1	5	6	3	2	5	11
1955	3		3	2		2	5
1956	2	5	7	5	2	7	14
1957	6	6	12	3	1	4	16
1958	7	1	8	1	2	3	11
1959	5	1	6	4	1	5	11
1960	4	5	9		2	2	11
1961	3	3	6	1	1	2	8
1962	2	3	5		1	1	6
	52	50	102	26	22	48	150



Standard age incidence

Fig 1

During the first 10 year period 50 cases occurred while during the latter period there were 100 or twice as many. This applies to the benign as well as to the malignant tumours. Accordingly the percental distribution of these two groups is the same.

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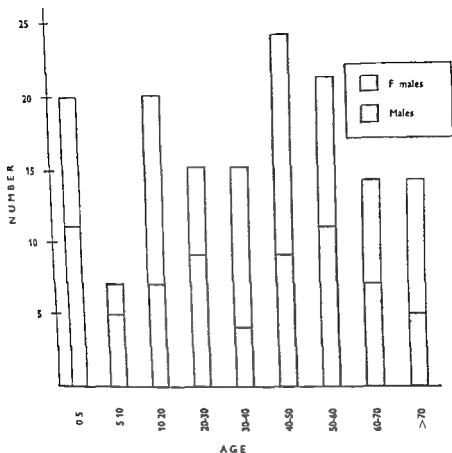
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1945	1	2	3		1	1	4
1946	4	2	6	1		1	7
1947	1	1	2		2	2	4
1948	1		1			0	1
1949	4	1	5	3		3	8
1950	1	2	3	1	2	3	6
1951	1	3	4	1		1	5
1952	2	1	3		1	1	4
1953	1	4	5		2	2	7
1954	1	5	6	3	2	5	11
1955	3		3	2		2	5
1956	2	5	7	5	2	7	14
1957	6	6	12	3	1	4	16
1958	7	1	8	1	2	3	11
1959	5	1	6	4	1	5	11
1960	4	5	9		2	2	11
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With the division into 10 year age groups it will be seen that the number of tumours was largest from 0 — 10 years, a total of 27. The most common

tumours in this age group were dermoid cysts and gliomas of the optic nerve, each of which made up 22%

A relatively large number of tumours occurred also in the age groups 40-50 and 50-60 in which particularly pseudotumours were predominant, making up 40% and almost 30% respectively

In all other age groups the distribution of the various types is more even

Table 2
Distribution of Orbital Tumours

	Benign	Malignant	Total	Per cent
Right	38	21	59	40
Left	62	20	82	54
Bilateral	2	7	9	6
Total	102	48	150	100

Table 2 lists the distribution of tumours in the right and left orbit. It shows a larger number of benign tumours in the left orbit. I am unable to say whether this is accidental. The malignant tumours were equally distributed. 6% were bilateral, and of the bilateral tumours three quarters were malignant, especially sympathicoblastomas and the group of lymphosarcomas leukaemia.

The orbit was divided into the space inside the muscle cone and the space outside. The latter was subdivided into 4 quadrants. The localization of the tumours is shown in Table 3. The most common site was supero-temporal where almost two fifths were situated. Out of these tumours more than one third were malignant, consisting mainly of malignant lacrimal gland tumours.

The upper nasal quadrant housed about one quarter, one fifth of which were malignant. The least common sites were the lower quadrants, the lower temporal quadrant housing 7% and the lower nasal quadrant only 5%. In the last mentioned quadrant two fifths of the tumours were malignant.

14% of the tumours occupied two quadrants. Only 40% of these growths were malignant. Only a very few were of diffuse localization.

Inside the muscle cone about one tenth of the tumours were situated, and of these almost three quarters were malignant. Gliomas predominated, making up 90%.

Histopathological Classification

For the histopathological classification I used a modification of Hogan & Zimmermann's (Table 4). The tumours were divided into benign and malignant.

Table 3
Localization of Orbital Tumours

Superior		Nasal	
Temporal			
Benign	39	Benign	28
Malignant	18	Malignant	6
$57 = 38\%$		$34 = 23\%$	
Benign	10	Benign	5
Malignant	1	Malignant	3
$11 = 7\%$		$8 = 5\%$	

Inferior	
Double localization	$\left\{ \begin{array}{l} \text{Benign} \quad 13 \\ \text{Malignant} \quad 8 \end{array} \right\} 21 = 14\%$
Diffuse localization	$\left\{ \begin{array}{l} \text{Benign} \quad 2 \\ \text{Malignant} \quad 1 \end{array} \right\} 3 = 2\%$
Inside muscle cone	$\left\{ \begin{array}{l} \text{Benign} \quad 5 \\ \text{Malignant} \quad 11 \end{array} \right\} 16 = 11\%$

The first group within the benign tumours is the choristomas. These tumours are made up of tissue components which are not normally present in the site. Here dermoid cysts predominated.

A hamartoma is tumour like growth of tissue which normally occurs in the site concerned. Within this group haemangiomas were common.

However the most common benign tumour was pseudotumour, a total of 29 cases. Together with the dermoid cysts the pseudotumours made up more than half of all the benign tumours.

Benign mixed tumours of the lacrimal gland occurred in 4 cases. Out of these tumours three became transformed into malignant mixed tumours after the lapse of 4, 10, and 12 years. The remaining tumour has not shown signs of malignancy after 11 years follow up.

Within the malignant group gliomas of the optic nerve, lacrimal gland tumours, and embryonic sarcomas were most common, comprising together more than half.

Embryonic sarcomas are often called rhabdomyosarcomas, even though no striation is observed, and I doubt whether this designation is correct.

All gliomas of the optic nerve were assigned to malignant tumours. This is perhaps a matter of discussion. Biologically these tumours usually behave as benign, but as they all show invasive growth, though slow, and as they kill their host if untreated, I prefer to classify them as malignant.

Table 4
Histopathological Classification

	<i>Benign</i>	<i>Number</i>	<i>Malignant</i>	<i>Number</i>
<i>Choristomatous</i>	Dermoid cyst	23		
	Epidermal cyst	1		
	Teratoma	1		
<i>Hamartomatous</i>	Haemangioma	11	Haemangiosarcoma	2
	Sclerosing haemangioma	2		
	Haemangioendothelioma	1		
	Simple cyst	5		
<i>Mesenchymal</i>	Fibroma	2		
	Lipoma	4		
	Myxoma	1	Myxosarcoma	2
	Osteoma	4		
			Embryonal sarcoma	6
			Reticulum cell sarcoma	4
<i>Neurogenic</i>	Schwannoma	7		
	Neurofibroma	5	Neurofibrosarcoma	1
	Meningioma	4		
			Glioma of optic nerve	10
			Sympathicoblastoma	3
<i>Epithelial</i>	Benign mixed tumour of the lacrimal gland	(4)	Malignant mixed tumour of the lacrimal gland	1
		1	3 transformed to Malignant mixed tumour of the lacrimal gland	3
			Aderoid cystic carcinoma of the lacrimal gland	3
			Carcinoma of the lacrimal gland	2
<i>Inflammatory (pseudotumours)</i>	Lymphoma	6		
	Localized inflammatory reaction	23		
<i>Systemic diseases</i>	Sarcoidosis	1		
			Lymphosarcoma-leukaemia	8
			Myelomatosis	1
			Reticuloendothelioses	2
Total		102		48

Sympathicoblastomas were included in the present classification, even though they are not primary. This was done because as a rule the first clinical sign of these tumours appears in the orbit, and in most cases the

diagnosis is made on the basis of a biopsy from the orbit. It is important, therefore, that the ophthalmologist should bear this disease in mind.

Within the group of reticuloendothelioses there is one case of Letterer-Siwe's disease and one of disseminated xanthogranulomatosis.

Treatment

The treatment of the malignant tumours and the result thereof is apparent from Table 5. The analysis was concluded on 31.12.1967. 11 cases were treated by exenteration, some of them combined with radiation. This was used mainly for cases of embryonic sarcoma and lacrimal gland tumours. 9 eyes were enucleated, usually in combination with extirpation of optic nerve gliomas.

Although the material is too small to justify conclusions concerning the most favourable treatment, the findings and the impression from the remainder of the material indicate the following. For embryonic sarcomas and malignant lacrimal gland tumours the prognosis is poor. Even a procedure as extensive as exenteration, possibly combined with radiation, does not afford better results than extirpation of the tumour, possibly combined with radiation.

For gliomas of the optic nerve the prognosis is relatively favourable after extirpation. However, it is often necessary to perform enucleation as well.

The treatment of the group lymphosarcoma/leukaemia indicates that radiotherapy alone affords equally good results as radiotherapy combined with operation.

Follow up

Table 6 gives the survivals 5 and 10 years after the histological diagnosis. Within the 10 year survival time 5 patients had to be excluded because the follow up period was too short.

At the end of 5 years two fifths and at the end of 10 years more than half the patients had died of their tumours.

Patients with embryonic sarcoma usually succumb within the first couple of years, while patients with malignant lacrimal gland tumours survive for a fairly long time. At long sight, however, the prognosis in this group too is poor because of the repeated recurrences of an increasingly malignant nature. Within 10 years two thirds of the patients had died of their tumours. However, a follow up period of 10 years is too short for a final evaluation.

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Table 6
Follow-up of the Malignant Tumors 15

	Number	Dft	5 Years Dfc	Alive	Number	Dft	10 Years Dfc	Alive
Hemangiosarcoma				2	1			1
Myxosarcoma	2	1		1	1	1		
Embryonal sarcoma	6	4		2	6	5		1
Reticulum cell sarcoma	1	1	2	1	4	2	2	
Neurofibrosarcoma	1			1	0			
Glioma of optic nerve	10	1		9	8	2	1	5
Sympathicoblastoma	3	3			3	3		
Malignant mixed tumour of the lacrimal gland	4			4	4	1		3
Adenoid cystic carcinoma of the lacrimal gland	3	2	1		3	2	1	
Carcinoma of the lacrimal gland	2	1	1		2	1	1	
Lymphosarcoma leukaemia	8	3	1	4	8	5	1	2
Myelomatosis	1	1			1	1		
Reticuloendotheliosis	2	2			2	2		
Total	48	10	5	24	43*	25	6	12

Symbols: Dft = dead from tumour
Dfc = dead from other cause

* 5 excluded for statistical reasons

Table 5

Therapy and Outcome of the Malignant Orbital Tumours

	Exstirpation			Exstirpation + Radiation			Exstirpation + Radiation			Radiation			Cytostatics			No Treatment
	Dt	Dc	A	Dt	Dc	A	Dt	Dc	A	Dt	Dc	A	Dt	Dc	A	
Haemangiosarcoma							1		1							
Myxosarcoma				1					1							
Embryonal sarcoma				+1*				3		1						
				1												
Reticulum cell sarcoma				1						2	1					
Neurofibrosarcoma				1												
Glioma of optic nerve	1	3	1	1	2											1
			+1													
Sympathicoblastoma	1									1				1		
Malignant mixed tumour of the lacrimal gland				1	1				1	1						
Adenoid cystic carcinoma of the lacrimal gland	1			1												
Carcinoma of the lacrimal gland																
										1	1					
Lymphosarcoma- leukaemia	2	1		2									1	1*		1
Myelomatosis																
										1						
Reticulo endothelioses										1						

Symbols Dt = dead from tumour

Dc = dead from other cause

* + cyto tat .s

From the Eye Clinic Bispebjerg Hospital Copenhagen
Head E Godtfredsen M D

NEURO OPHTHALMOLOGIC FOCAL DIAGNOSIS

By

Erik Godtfredsen

Ophthalmologic signs and symptoms occur at an early stage and are also frequent in patients with intracranial tumours. Such have been found in from one half to two thirds of the patients. Many patients consult primarily an ophthalmologist with their complaints. If choked disc, the chiasmal syndrome, or ophthalmoplegia is found it is up to the ophthalmologist to get started the series of examinations which may result in an adequate diagnosis and therapy. As many neuro ophthalmic diseases may threaten both vision and life ophthalmologists become greatly responsible for the welfare of these patients. The tasks of the ophthalmologists may be formulated as follows:

- 1 make the diagnosis and after sorting of the patients refer these to special clinics
- 2 contribute towards focal diagnosis, and
- 3 follow up the patients to watch them with a view to a suitable remission rate after instituted therapy, give notice in case of recurrence

How often, when and how can the ophthalmologist contribute towards a focal diagnosis?

The conditions relating to intracranial tumours being the most important and also those most thoroughly studied there may be reason to concentrate particularly on these.

The incidence and the value of localizing the various ophthalmologic symptoms in relation to intracranial tumours will be dealt with first.

It is seen in table 1 that although choked disc is an extremely frequent and important cardinal sign of an intracranial tumour it is a highly problematic one where focal diagnosis is concerned. This is true of both uni- and bilateral choked disc and in the case of Foster Kennedy's syndrome (Wovern).

Conclusion and Summary

Although orbital tumours are relatively uncommon in Denmark, averaging 7 or 8 cases per annum in an average population of about 4.4 millions, these tumours do deserve a great deal of attention.

In respect to treatment two factors should be emphasized. Although a growth is histologically a benign looking mixed tumour of the lacrimal gland, it should be considered potentially malignant and treated by radical measures (radiotherapy + extirpation + possibly bony resection of the orbital roof), as the study showed that 75% of these tumours underwent malignant transformation in the course of some years.

Moreover, it may be impossible to distinguish histologically a benign lymphoma from a lymphosarcoma or an infiltration as a link in lymphatic leukaemia. In every case, therefore, relevant clinical studies should be performed to detect systemic disease, and the patient should be closely followed.

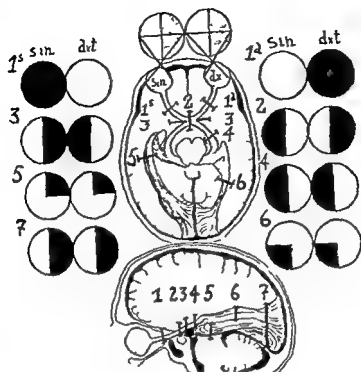


Fig 1

Visual field changes following lesions of different sections of the optic nerve path

lead to tragic mistaken diagnoses (Bardram & Møller, Enoksson) The chiasmatic syndrome accounts for 15 per cent of all visual field defects. It is worth pointing out that the differential diagnostic reflections in the presence of atypical chiasmatic syndromes should include simple glaucoma which may occur simultaneously with pituitary tumours (Godfredsen 1968).

4-7 Lesions of the longest section of the visual path from the chiasm to and including the visual cortex are associated with a contralateral homonymous hemianopsia, the most frequently occurring form of hemianopsia. The most important form from a local diagnostic aspect is the homonymous upper quadrantanopsia, which is a typical finding in relation to the temporal lobe tumours, being observed in one fifth of the patients, according to Edmund's thorough investigations. As is well known, quadrantanopsia is due to lesion of Meyer's loop, the lower and ventral portion of the optic nerve path, which winds forwards and round the temporal part of the lateral ventricle. The possible diagnostic value of the

Table 1

Frequency and focal diagnostic value of eye signs and symptoms in cases of intracranial tumors

	Frequency	Focal diagnostic value in per cent
Choked disc	60-70	?
visual field defects	40	25
ophthalmoplegias	16	4
pupil anomalies	15	5

Visual field changes, on the other hand, play a very important part. On this basis the ophthalmologist can yield weighty focal diagnostic information in 25 per cent of the cases by demonstrating presence of the chiasmal syndrome and homonymous upper quadrantanopsia. Ophthalmoplegia of the infranuclear type and pupillary changes each occur in 15 per cent of patients with intracranial tumours, but these are only in a fairly small number (one fourth — one third) of focal diagnostic value, e.g. in cases of concurrent ophthalmoplegia of the cavernous sinus type. Rarer symptoms, such as paralysis of gaze, nystagmus, exophthalmos, each contribute only modestly to a focal diagnosis. These symptoms will not be further discussed in this place.

Considering all the ophthalmologic signs and symptoms collectively, they can be said to yield focal diagnostic information in about one third of the patients.

When and how can the ophthalmologist contribute towards focal diagnosis on the basis of visual field defects?

Fig. 1 illustrates in diagrammatic form the correlation between visual field defects and corresponding lesions of the optic nerve path.

1 *Optic nerve lesions* with unilateral visual field defects are met with in cases of traumatic optic nerve lesions (Edmund & Godfredsen) and temporal arteritis, for instance, both with the well known poor prognosis, unlike the conditions relating to retrobulbar neuritis.

2 In the presence of *chiasmal affections* ophthalmologists can contribute essentially towards a focal diagnosis, even though the optic chiasm comprises a small section only of the total visual path. The chiasmal syndrome, with optic nerve atrophy and bitemporal hemianopsia, is most frequently seen in association with chromophobic pituitary adenomas, which constitute 10 per cent of all intracranial tumours, as well as meningiomas from the tuberculum sellae, and craniopharyngiomas, each representing 2 per cent. The two latter tumour forms may be accompanied by atypical chiasmatic syndromes with asymmetric visual fields and running an unpredictable, almost intermittent course, which may

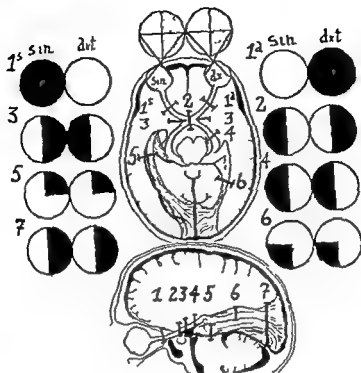


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congruity and macular sparing of the visual fields will not be discussed in this place, the observations made being by no means univocal. Reference is made to papers by Enoksson, Huber, Harrington, and Walsh.

Significance of ophthalmoplegia in focal diagnosis

Ophthalmoplegia of the infranuclear type occurs more or less frequently in association with the various neuro ophthalmic diseases. This symptom is relatively rare in relation to such common diseases as cerebral apoplexy and head injuries (present in 2–10 per cent), whereas more frequent in the comparatively rare diseases, such as intracranial aneurysms (present in 30 per cent, chiefly in the form of oculomotor nerve palsy). As stated, 16 per cent of patients with intracranial tumours present ophthalmoplegia. The incidence of this combination is the same in large series of ophthalmoplegia patients. Thus, *Rucker* (1958, 1966) found that half of all ophthalmoplegia cases are equally distributed between patients with intracranial tumours, head injuries, and vascular diseases. While solitary ophthalmoplegia, with abducens nerve palsy predominating, is of relatively low focal-diagnostic value, combined ophthalmoplegias in the form of a more or less complete cavernous sinus syndrome (ophthalmoplegia and trigeminus I lesion) are of great value. Combined ophthalmoplegias are found in from one fourth to one third of patients with intracranial tumours. 10 per cent of the pituitary tumours — depending on extrasellar tumour growth — are associated with ophthalmoplegia (*Bardram*), while in 20 per cent of the patients with malignant nasopharyngeal tumours invading the middle cranial fossa we find a cavernous sinus syndrome (*Godtfredsen & Ledermann*).

Conversely, in a series of patients with the cavernous sinus syndrome (*Jefferson*), this is in the same percentages of cases caused by pituitary tumours and nasopharyngeal tumours respectively, as shown in table 2.

Table 2
The aetiology in 112 cases of the cavernous sinus syndrome (Jefferson)

Tumors		52 cases
nasopharynx	23	
Pituitary	11	
Aneurysm		38 cases
sacculate	29	
Traumatic		22 cases
carotid fistula	17	

Summary and Conclusion

In patients with neuro ophthalmic diseases especially intracranial tumours, such ophthalmologic signs and symptoms as choked disc, visual field defects and ophthalmoplegia are frequent (present in 50-60 per cent) and occur at an early stage

The ophthalmologic symptoms become of local diagnostic importance in one third of the patients, choked disc and solitary ophthalmoplegia being of no value from a localizing aspect. Visual field defects of the type of chiasmal syndrome and homonymous upper quadrantanopsia, as well as combined ophthalmoplegias (the cavernous sinus syndrome) are of great importance in the local diagnosis. The ophthalmologists can contribute largely towards localizing the tumours situated at the base of the skull, where neuroradiology is a less supreme diagnostic aid.

REFERENCES

- Bardram M and H U Møller: Diagnosis of tumours. *Acta Ophth* 30: 65 1952
Bardram M: Oculomotoric pareses in pituitary adenomas. *Acta Ophth* 27: 225 1949
Edmund J: Visual disturbances with gliomas of the temporal and occipital lobe. *Acta Psych & Neurol* 29: 291 1954
Edmund J and Godfredsen E: Unilateral optic atrophy following head injury. *Acta ophth* 41: 693 1963
Enoksson P: Perimetry in neuro-ophthalmological diagnosis. *Acta ophth Suppl* 82: pp 54 1965
Godfredsen E: Studies on the cavernous sinus syndrome. 1. Incidence of infranuclear ophthalmoplegias. *Acta Neurol Sc* 40: 69 1964
Godfredsen E and Ledermann M: Studies on the cavernous sinus syndrome. 2. Ophthalmoneurologic signs in malignant nasopharyngeal tumors. *Acta Neurol Sc* 41: 43 1965 and *ibidem* *Americ J Ophth* 59: 1063 1965
Godfredsen E: Glaucoma and pituitary tumor. *Acta ophth* 46: 600 1968
Harrington D: The visual field. A text book. 2 ed. Mosby St. Louis, U.S.A. 1964 pp 386
Huber A: Augensymptome bei Hirntumoren. Huber, Bern 1956 pp 403
Jefferson G: The cavernous sinus syndrome (Bowmann lecture). *Transact Ophth Soc U.K.* 73: 117 1953
Rucker C W: Paralysis of the third, fourth and the sixth cranial nerve. *Amer J Ophth* 46: 787 1958
—: The causes of paralysis of the third, fourth and sixth cranial nerve. *Amer J Ophth* 61: 1293 1966
Wash F B: The ocular signs of tumors involving the anterior visual pathway. *Amer J Ophth* 42: 347 1956
Wassermann F: The Foster-Kennedy syndrome. An evaluation of its diagnostic value. *Acta Neurol Sc* 43: 205 1967

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PUPILLOMOTORIC PERIMETRY IN PSYCHOGENIC DEFECTS OF THE VISUAL FIELDS

By

Paul Enoksson and Barbro Hallen

In 1956 Harms presented an extensive study on the possibilities of pupillomotoric perimetry. He pointed out that this was of no value in topical diagnosis as all field defects due to organic lesions change the pupillomotoric response irrespective of the location of the lesion. He stressed, however, that it could be used for differentiating between organic and functional visual disorders. The clinical value of this statement, which does not seem to have attracted the attention it really deserves, is illustrated by the following two cases.

Case Reports

Case 1 A K Y, woman aged 23, worked for some time as a nurse and later as technical assistant in X-ray work. Four years earlier concussion of the brain and after that several attacks of fainting. These disappeared after half a year but reappeared 8 months before the present illness. One day when occupied with sorting berries she suddenly reported loss of vision. She could, however, move through the room without difficulty. After a while she fainted. When awake again she complained of headache. Eye examination performed the next day. A slight temporal defect recorded in the left visual field. Five days later admitted to hospital.

Examination Uncharacteristic disturbances of coordination.

Electroencephalography Unspecific abnormality on the right temporal side.

Ocular findings Vision was 1.0 bilaterally. Perimetry showed increase of the left visual field defect. A restriction of the temporal periphery was recorded combined with an absolute scotoma extending to the left from 5 to 20 degrees from the fixation point.

Carotid angiography was performed on both sides and showed no signs of disease. The anterior communicating artery and the posterior cerebral arteries did not fill, however.

The patient left hospital after three weeks. Two months later admitted

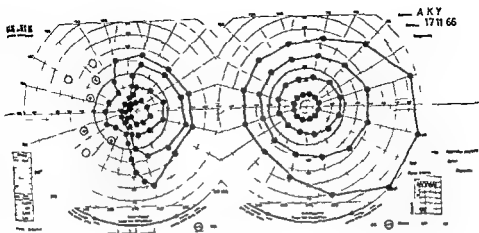


Fig 1

to a neurological clinic after sudden loss of consciousness lasting 5 or 6 minutes. Complained of supraorbital pain on the right side.

Right carotid angiography performed again. This time the anterior communicating artery did fill. Suspicion of aneurysm not confirmed. At the end of the angiographic procedure the patient reported numbness and weakness on the left side of the body. When examined immediately afterwards she appeared to have left sided hemihypaesthesia and almost complete left sided hemiplegia with the exception of the facial muscles.

Electroencephalography two days later showed a more pronounced abnormality on the right side than earlier, thus indicating the occurrence of brain damage during angiography.

Ocular findings Two days after the angiography visual field examination was performed with the perimeter of Goldmann. Peripheral left sided restriction was recorded in both fields and with a weak stimulus complete left sided hemianopia was found in the right eye and a left sided paracentral scotoma in the left. A week later the right field appeared normal but the left field showed now almost complete temporal hemianopia. Another week later the right field seemed completely normal when studied in detail but the left sided temporal hemianopia persisted (Fig 1). However, when the latter finding was controlled by switching on and off the largest and most intense test object in different parts of the left visual field, it was observed that it produced pupillary contractions even from points within the defective part of the field. As this finding was not compatible with an organic lesion the test was repeated some days later and now in a more systematic way.

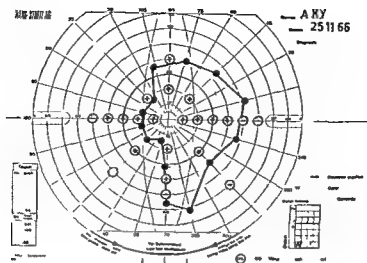


Fig 2

Pupillomotoric perimetry The perimeter of Goldmann was used this time also and with the standardized background illumination. The left visual field was first examined with kinetic perimetry. A temporal field defect was recorded as before. Pupillomotoric perimetry was then performed with the largest and most intense test object. The pupillary contractions were symmetrical in all tested meridians, extending to 40 degrees from the fixation point temporally as well as nasally. The patient's verbal reports were also recorded (Fig 2).

Course At the time when the pupillomotoric perimetry was performed, the cutaneous sensibility had already turned normal. The hemiparesis varied in an unpredictable manner, was not accompanied by any disturbances of peripheral reflexes and disappeared completely within 10 months. As the patient did not complain of visual disturbances any more, the visual fields were not re examined.

Case 2 A T, girl aged 10. Lost her father in an accident at the age of 2. Had a younger sister and after her mother's second marriage also a half sister. When the girl was eight her family moved and she was brought to a new school. Soon afterwards she complained of visual deterioration and was allowed to change her seat in the classroom, gradually getting farther and farther forward. Her physical development was more rapid than that of her schoolfellows, mammary growth starting at the age of eight and a half. This made her feel embarrassed in the other children's company.

Ocular findings Right visual acuity 0.1 and did not change with glasses. Left visual acuity 0.1 without correction and 0.2 when two spherical

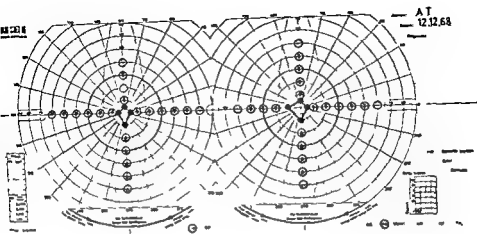


Fig 3

glasses of equal strength but opposite sign was used. She could read Jaeger no 3 binocularly. Though perimetry showed marked constriction of the visual fields she moved freely at the ward (Fig 3).

Pupillomotoric perimetry. This was performed with the same technique as in Case 1. Pupillary contractions were obtained within the field of either eye to a distance of 40 degrees or more from the point of fixation both in vertical and horizontal meridians (Fig 3).

Course. The visual disturbance has persisted during an observation time of 6 months. During this period menstruations have begun.

Comments

The diagnosis of functional neurological disturbances is usually based on indirect evidence. This is also true of psychogenic defects of the visual fields. When the fields have a spiral form or are extremely constricted though the patient has no orientation difficulties this may be taken as signs of functional disturbance. Pupillomotoric perimetry may sometimes prove the functional character of the field defect as in the first of the present two cases. The almost complete left temporal hemianopia without any restriction of the right field indicated a lesion of the retina or the optic nerve. This could however not be verified at pupillomotoric perimetry. Nor did the concentric restriction of the fields in Case 2 appear with this technique. This finding may suggest bilateral lesions of the intracerebral visual pathway though this diagnosis seems improbable.

The sensitivity of the pupillomotoric response varies widely in different individuals but is usually high at early ages when psychogenic visual

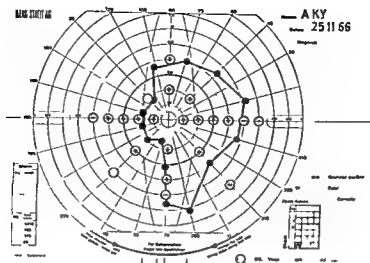


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THE SHAPE OF VISUAL FIELDS IN NORMAL SUBJECTS

By

A. Egge

To be published in Acta Ophthalmologica

disorders are prone to appear. The present study shows that the instrument of Goldmann may be convenient for pupillomotoric perimetry when used with its standardized background illumination.

Summary

Two cases are described, illustrating the value of pupillomotoric perimetry when psychogenic field defects are suspected, and showing that the perimeter of Goldmann is well suited for this technique.

REFERENCE

1. Harms H. Möglichkeiten und Grenzen der pupillomotorischen Perimetrie. *Klin. Mbl. Augenheilk.* 1956; 129: 518-534.

Discussion

G. von Bahr (Uppsala)

When evaluating the pupillary reaction after light stimulation of a blind part of the visual field, one has to bear in mind that the macula area has a much greater pupillomotoric sensitivity than the rest of the retina. Light rays deflected from the lens substance and from the retina itself may therefore produce a pupillary reaction even if the light has been focused and directed against a blind spot of the retina. When doing these tests one therefore has to insure a constant macular illumination the same way as it is done with the hemikinesimeter.

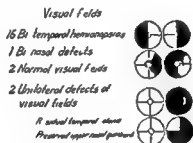
P. Enochsson

As no pupillary contraction appeared when the test object was projected within the blind spot, scattered light from peripheral parts of the eye ground to the macular region cannot explain the findings.

Only 11 patients had pneumo encephalography performed preoperatively. One might wonder that only half of the patients had a pneumo encephalography performed as it is known that especially the structures related to the chiasma are shown very clearly by this method, when it is performed with midline laminography using horizontal radiation.

However, after hormone examinations, roentgenograms of sella, ophthalmoneurologic examination and cerebral angiography the indications for craniotomy were so evident that a pneumo encephalography was not found necessary in all patients.

All patients had an ophthalmoneurologic examination performed preoperatively and the visual fields were found as follows:



Thus five of 21 patients had visual fields differing from the classic bitemporal defect of chromophobe adenoma of the pituitary gland, a defect Chamlin, Davidoff & Faring³ reported in 96 per cent of all cases.

One female showed a binasal defect in the visual fields as shown in Fig 1. In the same patient a bilateral excavation of the optic discs forced us to attempt the diagnosis of glaucoma sine tensio, as all glaucoma provocation tests were negative.

X-ray of sella turcica and the angiography were normal. Also no signs of dyscrine function were demonstrated. But a pneumo encephalography performed later suggested suprasellar tumour and the operation revealed a large chromophobe adenoma.

Roentgenograms of the two patients with normal visual fields showed a rather enlarged sella turcica. Carotis angiography showed displacement of the internal carotid as well as an elevation of the first part of the anterior cerebral artery.

In the patient with a residual temporal island of one eye and a normal visual field of the other eye a similarly enlarged sella turcica was found. Moreover, angiography showed suprasellar growth with displacement of the internal carotid and also of the anterior cerebral artery.

The patient with a preserved upper nasal quadrant on one side and a

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CHIASMAL VISUAL FIELDS

By

P M Møller and O Hvid Hansen

Supported by the Cold Stores Fond and OABS Fond, Odense

Chiasmal Visual Fields

The misinterpreting of chiasmal diseases is very likely to occur, but the possibility of correct diagnosis is however large if one takes the advantages of the many methods of investigation at disposal of ophthalmologists, physicians and neuroradiologists

In Scandinavia this has been emphasized in reports by *Larsson & Nord*,¹¹ *Bardram & H U Møller*,¹² *Hyllested & P M Møller*¹³

Studying the chiasmal syndrome one is constantly surprised by new aspects of the symptomatology

In Odense we examined records of patients with verified chromophobe adenoma with suprasellar extension, and we tried to correlate the results of the ophthalmologic examinations with the neurosurgical findings by operation and by neuroradiology

The material is small, but rather surprising, justifying the following discussion of certain factors in the pathogenesis of the defects in the visual fields

Material

The material includes 21 patients, aged 15-73 years. Twelve had symptoms of disturbed pituitary gland function

All patients had X ray examination of the skull performed and in all except one an enlarged sella turcica was demonstrated

Preoperatively a unilateral carotid angiography was performed in 18 patients, and in three cases bilateral examination was done. The angiography was mainly performed for estimating the position of the vessels in relation to the tumour, chiefly for surgical reasons. But furthermore reliable signs of a suprasellar space occupying lesion were found in 15 patients

- 2 The subsequent inferior bitemporal defect is caused by the growing tumour and the chiasmal displacement against the anterior communicating artery

*Hearns & Rucler*¹⁶ interestingly showed in their study comprising four patients with typical arcuate visual defects of nerve lesion type that the defects were caused by chromophobe adenoma. Three of these patients had atrophic discs and one had normal optic nerves. All patients had an enlarged sella turcica.

These authors cannot exactly explain the development of the defects, but perhaps even ordinary bitemporal defects have more of a vascular basis than is usually supposed, and are not altogether due to direct mechanical pressure.

In 1962 *Hejt*⁷ published a study in which he in monkeys by destruction of the papillo macular bundle with photocoagulation was able to follow the course of these special fibers through the optic nerve and the chiasma. He concluded, that the lower arcuate bundle is located laterally and inferiorly in the optic nerve and uncrossed fibers of the lower arcuate bundle remained inferiorly and laterally in the chiasma. The superior arcuate bundle enters the chiasma superiorly and laterally. The structure of the chiasma is almost identical in the anthropoid ape and in man.

From his great knowledge of the chiasmal vascular supply and its variability *Hughes*⁸ cannot explain the defects in the visual fields as only based on vascular lesions.

*Francois & Neetens*⁴ who especially investigated the optic nerve and the chiasmal vascular structure are more inclined to explain that the view field loss is nearly always due to the mechanical effect of compression rather than to vascular obstruction.

Discussion

For two reasons we also are most inclined to explain the defects in the visual fields as being caused by mechanical compression of the nerve fibers in the optic nerve and in the chiasma.

- 1 The classic bitemporal defect is related to a tumour the location of which naturally may explain the visual defect.
- 2 The nerve fibers of the optic nerve should be regarded as ordinary myelinated fibers losing their conductivity during a variable period if exposed to pressure. Compression of short duration of the chiasma in a patient with chromophobe adenoma may lead to uni- or bilateral amaurosis. Postoperatively we have experienced full recovery of vision and of visual fields. This would not be possible if a loss of vision of this extent was caused by a total vascular obstruction.

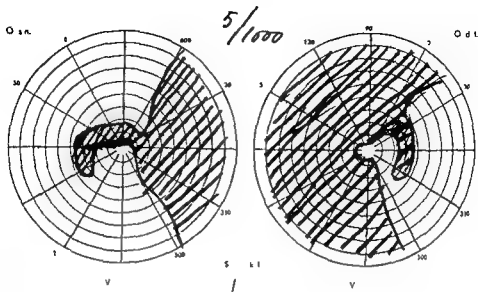


Fig 1

normal visual field on the other is not a frequent finding, however, not extremely infrequent either (Hughes⁴)

If these five patients are compared with the patients with typical bitemporal visual defects, it is, through our examinations and operative findings, obviously difficult to explain the large variation in the defects in the visual fields, and it is still more difficult to explain their development

Literature

H U Møller¹⁰ reported a case of binasal visual defects and excavated optic discs in a patient with normal tension, in whom operation revealed a chordoma from clivus Blumenbachii

Francois⁵ reviewed the literature and found 49 cases of binasal visual defects and reported further three cases. He concluded that a displacement of the third ventricle might displace the optic nerves towards the anterior cerebral arteries and the anterior communicating artery. Also a tumour in the region of the pituitary gland might produce a similar compression of the optic nerves, and finally a chiasmal arachnoiditis might cause a similar defect in the visual fields.

Hirsch⁶ mentioned two phases in the development of the bitemporal hemianopsia

- 1 The pressure of the tumour upwards against the chiasma produces the initial superior defect



Fig 2

photo of a chromophobe adenoma with an elevated and distended chiasma
surprisingly with normal visual fields

In 1962 *P M Moller* in Danish Society of Ophthalmology reported a patient with bilateral amaurosis caused by compression of the chiasma by a meningeoma from diaphragma sellae. The tumour was so small that the chiasma was hardly elevated. *Hughes*⁸ stated, that the chiasmatal vascular supply originated from the anterior cerebral artery and from branches directly from the internal carotid. According to the angiography, these vessels were normal, and also a normal position of the chiasma was found at operation. In this case compression of a fixed chiasma upon a tight diaphragma sellae might explain the visual defect.

In our opinion the large nasal defects in the visual fields of nerve lesion type might be explained purely mechanically. Operation revealed a highly elevated and tight chiasma with a marked open angle between the optic nerves. Due to this the lateral superior and inferior fibers in the optic nerves might be compressed against the optic foramina. This hypothesis is in accordance with the findings from the degeneration experiments by *Hoyt*.⁷ The visual defects of nerve lesion type observed in four patients by *Kearns & Rucker*¹⁰ might be explained similarly.

Also the reported case of unilateral visual defect with preserved upper nasal quadrant only might be explained according to the experimental study by *Hoyt*.⁷ In this case the pressure may elevate one of the optic nerves medially against the solid margin of the optic foramina.

We have no explanation of the exceptional case of a unilateral residual temporal insular visual field.

*Traquair*¹³ mentioned the temporal insular visual field in a case of an otherwise characteristic bitemporal hemianopsia. A number of nasal fibers running uncrossed through the chiasma might explain this case, but cannot explain the case reported by us.

It is difficult to explain why two of our patients with large suprasellar chromophobe adenomas had no defects of the visual fields when one sees the picture taken during the operation of one of the patients (Fig. 2).

The large tumour raises the optic nerves upwards and forwards, and all possibilities to give a purely mechanical defect of the visual field are present.

We know that the position of the chiasma varies greatly in relation to the sella turcica both with regards to the location in relation to tuberculum sellae and dorsum sellae and the vertical location of the chiasma relative to the diaphragma sellae.

Thus one can visualize a backward displaced high situated chiasma where only a very large tumour would cause pressure on the chiasma resulting in defects of the visual fields for purely mechanical reason.

In our opinion the hypothesis of the importance of the vascular ob-



Fig. 2

A photo of a chromophobe adenoma with an elevated and distended chiasma surprisingly with normal visual fields

struction for the development of bitemporal visual defects is not supported by the following reasons

- 1 Our material includes several patients with a highly reduced vision, as for instance only consisting in finger counts and hand movements. In spite of a large tumour with marked elevation of the anterior cerebral artery not the least defect of visual fields crossing the mid-line is demonstrated in these patients. In these cases the vessels supplying the anterior part of the chiasma are markedly tight and extended, making obstruction highly possible.
- 2 Should a vascular obstruction be of any importance, also the vascular supply to the lateral chiasma fibers should be affected. It is hard to believe that only the vessels supplying the medial and the anterior parts of the chiasma should be affected by tumours of huge size.
- 3 According to the frequency of variation of the anterior half of the circulus arteriosus Willisii (Adachi¹) the occurrence of bitemporal hemianopsia in 96 per cent of cases with chromophobe adenoma (stated by Chamlin, Davidoff & Fering²) does not at all support a vascular genesis.

Summary and conclusion

Twenty one patients with verified chromophobe adenoma of the pituitary gland with suprasellar extension are reported.

The visual fields are discussed with special reference to five cases without bitemporal hemianopsia. An interesting case of binasal visual defect of nerve lesion type is especially emphasized.

It is concluded that most defects in the visual fields can be explained by purely mechanical pressure on the chiasma.

REFERENCES

- 1 Adachi B. Das Arteriensystem der Japaner Bd. I Kyoto 1928.
- 2 Bardram M and Møller H L. Diagnosis of tumours in anterior and middle cranial fossae. Acta Ophthal. 1952 30 63-36.
- 3 Chamlin M, Davidoff L M and Fering E H. Ophthalmologic changes produced by pituitary tumours. Am J Ophthal. 1955 40 353-368.
- 4 Franc J L. Hemianopsie Binoculaire. Ophthalmologica 1947 113 321-343.
- 5 Franc J and Vernet J. Vascularization of the optic pathway. Brit J Ophthal. 1974 58 472-.
- 6 Hirsch O. De bitemporale Hemianopsie. Wiener Klinische Wochenschrift 1963 79 344-346.
- 7 Hoyt W F. Anatomic considerations of arcuate scotomas associated with lesions of the optic nerve and chiasm. Bull. Johns Hopkins Hosp. 1962 111 57-71.

- 8 *Hughes, B* Blood supply of the optic nerves and chiasma and its clinical significance
Brit J Ophthal, 1958, 42, 106-125
- 9 *Hyllested, A* and *Møller, P M* Follow up on patients with a history of optic neuritis Acta Ophthalmologica, 1961, 39 655-662
- 10 *Kearns, T P* and *Rucker, C W* Arcuate defects in the visual fields due to chromophobe adenoma of the pituitary gland Am J Ophthal, 1958, 45 505-507
- 11 *Larsson, S* and *Nord, B* Klinisk bild av retrobulbarneurit vid intracranella tumorer Nord Med, 1947, 34, 1059
- 12 *Møller, H U* Symptomes simulant le glaucome, dans un chordome du clivus Blumenbachii Acta Ophthalmologica, 1939, 17, 20-27
- 13 *Traquair, H M* Clinical Perimetry, 6th Edition The C V Mosby Co, St Louis, 1949

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Head Professor B Laursen MD

NEURO OPHTHALMOLOGICAL PATIENTS WITH BITEMPORAL HEMIANOPSIA

(Follow up study on etiology)

By

D Ruse

The finding of bitemporal hemianopsia during a neuro ophthalmological examination will always arouse interest because, in many cases, it may involve an operable lesion in the region of the chiasm

However this is not always the case. A group of patients with hemianopsia were followed up particular importance being attached to the differential diagnostical difficulties which have been encountered in the patients in whom no cause of visual field defect was revealed initially

Material and methods

The patients were selected from those who during the period 1960-67 were admitted to the neurosurgical and neuromedical departments of the University Clinic Copenhagen and who, during examination in the Eye Clinic were classified as suffering from bitemporal hemianopsia. By this procedure the sample will quite evidently be selected because the great majority had been examined by an ophthalmologist prior to admission. Hereby visual field defects have been excluded, where other causes could immediately be established.

The primary technique applied at the visual field examination was campimetry with a 3 mm white and a 10 mm red test object placed at a distance of 1 metre from the patient's eye. In cases of doubt and for the follow up studies a Goldmann perimeter was also used.

During the above period 128 cases of bitemporal hemianopsia were recorded. In 34 of these cases the cause of the visual field defect was disputable and the 34 patients were summoned for follow up study. The appearance and development of the visual field defects in the individual disorders will be dealt with only sporadically.

Results

The distribution of the diagnoses appears in table 1

Tumours	95
Other diseases in optic chiasm and nerves	13
Anomalies in optic disc and retina	12
Uncertain diagnosis	9
Total	129

The large number of tumours can be explained by the fact that the patients were referred mostly from the neurosurgical department. The distribution of the tumours appears in table 2

Pituitary adenoma	75
Cranio-pharyngeoma	7
Meningeoma	7
Dermoids	2
Oligodendroglioma	1
Angioma	1
Metastatic carcinoma	1
Abscess	1
Total	95

By far the most frequent types of tumour affecting the region of the chiasm are pituitary tumours

The distribution corresponds roughly to that found by other workers

In the figure, two types of bitemporal visual field defects found in association with tumours of the pituitary body are shown: bitemporal scotoma and bitemporal depression in the visual field.

The 13 cases, in which the defect resulted from other lesions in the chiasm and the optic nerve, are distributed as appears in table 3

Optic atrophy, uncertain type	6
Trauma	3
Chiasmal arachnoiditis	2
Multiple sclerosis	2
Total	13

The group optic atrophy without known etiology was found to be inhomogeneous, and the visual field defects were somewhat irregular. Two cases with cecocentral scotomas were, presumable, tobacco alcohol

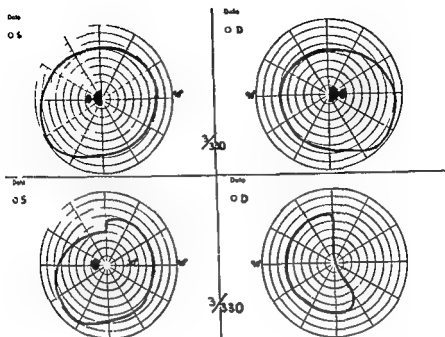


Fig 1

Bitemporal scotoma and bitemporal depression in the visual field in association with pituitary adenomas

amblyopias At the follow up examination some years later, the visual field defects in these two patients had not changed materially Consequently the existence of a tumour is rather unlikely although the possibility of slowly growing meningeoma cannot be excluded completely

In the group of opticochiasmatic arachnoiditis only histologically verified cases are included 11 cases in which the optic chiasm has been explored Presumably the incidence of this lesion has previously been over estimated and used as an exclusion diagnosis when no other causes of the bitemporal hemianopsia could be established

During the follow up period two patients developed typical multiple sclerosis

Disorders of the optic disc and the retina will often present difficulties as regards the differential diagnosis even if a diagnosis can be established by ophthalmoscopy The incidence appears from table 4

Ectasia of the fundus	8
Glaucoma	2
Drusen of the optic disc	1
Sectorial pigmentary retinal dystrophy	1
Total	12

Ectasia of the fundus is the most frequent source of error. The importance of knowing this differential diagnosis is emphasized by the fact that, in three of these patients, craniotomy and surgical exploration of the chiasm was performed because of the visual field defect.

The visual field defects result from localized ectasias in the nasal part of the retina. This makes the image of the test object on this part of the retina hazy and consequently, it is not perceived. By correction of the vision with minus glasses, the image can become clear, and the scotoma will disappear. In these cases the clinical picture is characterized by myopia, astigmatism, moderately impaired vision, inverted vessel emergence on the optic disc and inferior crescent. Bonamour and Schmidt explained this disorder which, in Scandinavia, was described by Enohsson, Odland and Ruse.

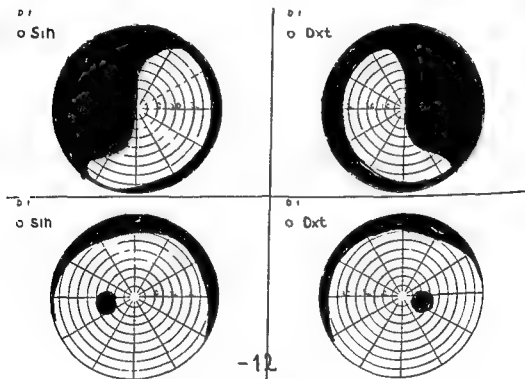


Fig 2

Bitemporal hemianopsia in fundus ectasia disappears after correction with minus lenses

In two cases, glaucoma caused the visual field defect, one of them in association with thrombosis of a retinal vein. In the other cases, where slight cataract was also present, the visual field defect almost disappeared after mydriasis.

In one case the visual field defect was caused, most likely, by drusen in the optic disc. Finally, one case of bilateral sectorial pigmentary retinal dystrophy in the nasal part of the retina was found.

In 9 cases no explanation of the defects could be established, see table 5

Check up not possible	3
Defects not found at check up	4
Uncertain nature	2
Total	9

The 4 cases which were not found again at check up, are small doubtful defects. In one case papilledema was present during the acute stage and the enlarged blind areas were presumably interpreted as being bitemporal hemianopsia.

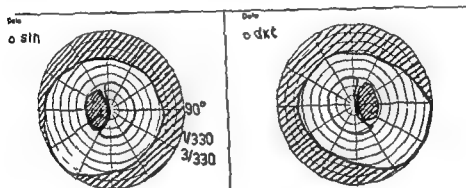


Fig. 3

Enlarged blind areas in papilledema simulating bitemporal hemianopsia

The last two cases represented visual field defects for small objects and had remained unchanged for some years without the development of optic atrophy.

Conclusion

Reviewing the results it may be said that they correspond roughly to the findings which would be expected in patients with bitemporal hemianopsia seen in a neuro-ophthalmological clinic (Walsh Traquair, Rucker). If a patient with bitemporal hemianopsia has reached as far as to a neurologic or neurosurgical department the most likely diagnosis will be pituitary tumour.

In cases of doubt exploration of the chiasm has been carried out, in some cases with negative results. On the other hand the check ups show that no tumours have been neglected.

Atrophy of the optic nerve occurring in some disorders i.e. multiple sclerosis and trauma may be associated with hemianopsia.

Although a number of disorders can be revealed by ophthalmoscopy, they have given rise to differential diagnostical difficulties. Of these, nasal fundus ectasias occurred most frequently and were most difficult to distinguish.

Summary

Over a 7-year period, 129 patients with bitemporal hemianopsia were encountered in a neuro ophthalmological clinic. The majority of these patients had tumours in the region of the chiasm. In 34 patients, no exact explanation of the visual field defects could be offered. These patients were summoned for follow up study 2-7 years later. The results of this study are reviewed.

REFERENCES

- Bonamour, Bregat, Bonnet, Juge: 'La Papille Optique' Masson & Cie, Paris 1968.
Bonamour et Leopold: Conf. Lyonnaises d'ophtalmologie Suppl. 1960.
Enoksson, P.: Perimetry in Neuro Ophthalmological Diagnosis. Suppl. Acta Ophthalmol. 82, 1965.
Odland, M.: Acta Neurol. Scand. 43: 630, 1967.
Ruse, D.: Acta Ophthalmol. 44: 906, 1966.
Rucker, C. W.: The Interpretation of Visual Fields. Am. Acad. of Ophth. and Otol. 1957.
Schmidt, T.: Ophthalmologica 129: 303, 1955.
Traquair, H. M.: An Introduction to Clinical Perimetry. Kimpton, London 6 ed. 1949.
Walsh, F. B.: Clinical Neuro Ophthalmology. Williams & Wilkins, Baltimore 1957.

Discussion

P. Ajer (Copenhagen)

I would like to thank Dr. Ruse for his interesting lecture. I would, however, like to bring to your attention the existence of a condition known as hereditary infantile optic atrophy. This dominantly inherited disease may in lightly affected cases only manifest itself by the presence of centro coecal scotomas. The heavily affected cases, however, shows a bitemporal bundle defect scotoma which can be confused with bitemporal quadrant anopsia. Dr. Ruse mentioned six cases where the etiology was uncertain and one of these had a centro coecal scotoma. A closer examination of the pedigree and family history of patients like this might elucidate the diagnosis.

From The Department of Experimental Ophthalmology University Eye Clinic Lund,
Sweden.

A MODIFIED PIEZO ELECTRICAL INSTRUMENT FOR OCULOSPHYGMOGRAPHY

By

H G Bynke, MD and R Öhman, Eng

A piezo electrical instrument for graphic recording of the corneal pulse has been introduced by *Bynke & Krakau (1964)*. This instrument has been demonstrated by *Bynke (1966, 1968)* and *Jensen (1968)* to be suitable for screening diagnosis of unilateral carotid occlusive disease where the amplitude of the corneal pulse wave is as a rule, less ipsilaterally than contralaterally.

The original instrument has certain disadvantages. The piezo electrical crystal is suspended in a plastic holder which is attached to a frame of balsa wood. During the examination the instrument hangs free on the bulb with one leg of the frame behind the head of the recumbent patient so that its centre of gravity lies beneath the contact surface on the cornea (see *Bynke & Krakau 1964 Fig 1*). The patient must therefore be placed on an examination table with his head on a head rest. If he is bedridden this is inconvenient since he has to be lifted from his bed for the oculospigmygraphy.

On the basis of experiments on rabbits *Bynke (1969)* concluded that in carotid obstruction a light instrument would be expected to produce a larger side difference of the pulse amplitude than a heavy one. Consequently there were reasons to try to reduce the weight of the instrument, which is 20 grams.

Another drawback of the method is the crystal's sensitivity to high frequencies. Small ocular movements, blinkings and other mechanical vibrations may disturb the shape of the recorded pulse curve so that measurements of the amplitude may be difficult in some cases. In order to improve the instrument some slight modifications have been performed.

The improved instrument

The instrument functions in the same way as the original one, and the piezo-electrical crystal and its plastic holder have not been changed.

The main modification consists in a change of the frame of balsa wood



Fig 1

The modified instrument hanging on the eye ball

The plastic holder is balanced by means of two short, vertical legs, one on each side of the head. The centre of gravity of the hanging instrument is still beneath the cornea, but since the lower, horizontal leg has been eliminated, the patient may remain lying in his bed at the examination (Fig 1). By diminishing the width and length of the frame, it has also been possible to reduce the weight from 20 grams to 10.

In order to reduce the signals caused by high frequency mechanical oscillations, a small capacitor (5600 pF) has been introduced parallel to the output of the crystal. This capacitor smoothens the curve but at the same time slightly reduces the amplitude of the pulse waves.

As yet, the modified instrument has been used only on a small number of patients, including 6 cases with unilateral carotid obstruction. In 5 of these the side difference of the pulse amplitude was found to be larger as recorded by this instrument than by the original one. Although the material is small, the results support the mentioned hypothesis that a light instrument is preferable to a heavy one for this diagnosis.

Summary

A modified piezo electrical instrument for oculosphygmography has been described. This instrument has certain advantages as compared with the original one. Above all, it is handier to use on bedridden patients.

REFERENCES

- Bynke H G and Krakau C E T A handy instrument for oculosphygmography with some clinical results *Ophthalmologica* 148 (1964) 367-373
- Bynke H G Screening diagnosis of carotid occlusion by means of oculosphygmography *Neurology* 16 (1966) 383-391
- Bynke H G Further estimation of the oculosphygmography as a diagnostic method in carotid occlusive disease *Acta Ophth* 46 (1968) 792-805
- Bynke H G Further studies on the ocular pulse in rabbits at experimental carotid occlusion and at loading of the bulb *Acta Ophth* 47 (1969) 514-522
- Jensen S Oculosphygmography *Acta Ophth* 46 (1968) 674-684

Discussion

W. Daaanger (Oslo)

What is the relation between the weight of measuring instrument and the absolute size of the pulsations? If the weight of the instrument decreases I would imagine that the size of the pulsations also will decrease. In other words pulsations caused by alteration of intraocular blood volume will result virtually no pulsations of the unindented cornea.

Are there any analysis elucidating the relation between size of pulsations measured by this method and the alterations in the intraocular blood volume?

Bynke (answer to Dr Daaanger) Due to deformation of the bulb the pulse amplitude decreases as the weight of the instrument increases. In rabbits the pulse volume has been found to be 1-2 cu mm.

From The University of Bergen, School of Medicine, Department of Ophthalmology
Head Professor *Torstein I Bertelsen, MD*

REGISTRATION OF ORBITAL PULSATIONS

By

Martin Davanger

The eye-ball is placed in the aperture of the orbit, and fills most of the opening. The periphery of the aperture is closed by the orbital septum.

Thus, the bulb may be considered a piston in the anterior part of the orbit. The orbital walls are bony and rigid. Therefore, volume changes of the content of the orbit will induce changes in the position of the eye ball, a volume increase will push the eye forwards, a decrease will bring it deeper in the orbit.

The arteries in the orbit have an increased volume in the systole as compared with the diastole, and there are also pulsations in the veins. The variations of the blood volume in the orbit will induce pulse-synchronous forward and backward movements of the piston in the anterior aperture, the eye ball.

In some pathological conditions the pulsatory movements of the eye ball are so large that the movements are easily seen and palpated. This phenomenon is called exophthalmus pulsans. It is said that in 90 per cent of these cases the cause is an arterio venous aneurysm in the cavernous sinus. In this condition the orbital veins have arterial blood pressure and pressure variations. The orbital veins have much larger volume than the arteries, and their wall is much more distensible. Therefore, in arterio venous aneurysm the pulse synchronous variations in the volume of the orbital content are considerably larger than the normal, and the forward and backward movements are consequently larger.

Another cause of exophthalmus pulsans is a defect in the bony wall between the orbit and the cranial cavity. In these cases the intracranial pulsations will be transmitted to the orbital content and the eye ball. Such defects may be congenital, in cases of orbital encephalocele, or may be caused by tumours in this region. Typical is a neurofibroma as a manifestation of neurofibromatosis, von Recklinghausen's disease.

A third cause of exophthalmus pulsans is highly vascularized orbital tumours. This condition may be mistaken for an arteriovenous aneurysm, as it may cause both visible pulsations of the eye ball, and pulse syn

chronous noise by auscultation, a phenomenon which is usually considered as indicating an arteriovenous aneurysm

In diseases of the orbit there are pulsations of any degree, from the small movements of the eye ball found in normal persons, to the large pulsatory movements which may easily be recognized by inspection and palpation, in which case the term *exophthalmus pulsans* is natural

In the diagnostic evaluation of a case of *exophthalmus* it may be of value to have a quantitative measure of the size of the orbital pulsations. This may give an impression of the vascularization of an eventual orbital tumour, and knowledge of this may be useful when planning and preparing an operation

Tuyl (1901) constructed an apparatus for graphical registration of the pulsatory movements of the eye ball in the orbit. The apparatus consisted of a two armed lever, with one short and one long arm. A small concave plate is attached to the short arm and this plate rests upon cornea. The long arm has a needle which can write on a sheet. The backward and forward movements of the eye are recorded on this sheet, in a magnification which is determined by the relation between the long and the short arm of the lever

With this apparatus it was found that the pulsatory movements of the eye ball in the orbit had a size of 0.01 to 0.02 mm in normal persons

The pulsations of the orbit have also been recorded by plethysmography. Wegner (1930) used a capsule which was fixed air tight to the orbital margin. The orbital pulsations induce pressure variations in the air in the capsule and the pressure variations are recorded

This method of course does not allow one to measure the size of the movements of the eye ball in mm. Another disadvantage is the difficulty in adapting the capsule air tight to the orbital margin in all cases

A new method will now be described by which the orbital pulsations are magnified and recorded by the use of a Schiotz tonometer as a linear transducer

In a mechanical tonometer the movements of the plunger are indicated by the pointer in 20 times magnification. By using an electronic tonometer further magnification is obtained, and the movements can be recorded on paper by a recorder as in tonography

When using a Schiotz tonometer for the registration of orbital pulsations the tonometer's handle and footplate must be fastened in relation to the cranium. This can be obtained with the help of Merte's tonometer holder which is constructed as an aid in tonography (Merte 1957). The holder consists of a plate which is attached to the patient's forehead by a band around the head. To this plate the tonometer can be fastened in any relevant position by a holder attached to the plate

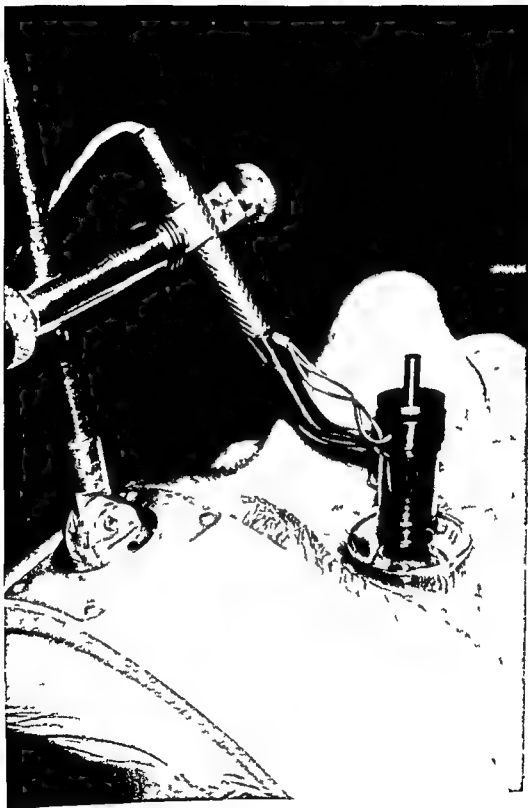


Fig 1

An electronic Schiotz tonometer held in position by Merté's holder. The plunger touches a contact lens on cornea.

The patient lies flat on his back (Fig 1) The eye is kept open by a Zeiss lid speculum A contact lens is placed on cornea, I have used +25 to obtain a sufficiently convex anterior surface The tonometer is lowered until the plunger, and only the plunger, rests upon the contact lens (Fig 2) The footplate should not touch the contact lens

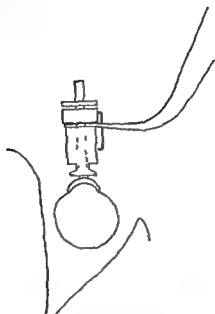


Fig 2

The principle of registration of orbital pulsations by the help of an electronic Schiotz tonometer

The movements of the eye ball are now transmitted via the contact lens to the plunger and thereby recorded by the recorder The size of the pulsations can be measured on the paper and converted into hundredths of millimeter as we know that one scale reading is equivalent to $1/20$ or $5/100$ mm

In Fig 3 is shown an example of a registration in a normal person The pulsatory movements are in normal cases about $2-3/100$ mm and very rarely as much as $5/100$ mm

Some registrations demonstrate respiratory movements of the eye in addition to the pulsatory These movements are usually of the same magnitude as the pulsatory

The shape of the pulsations is sometimes different from the rounded waves in Fig 3 The downward waves may have an acute form in others the waves have a less regular complex form as shown in Fig 4 In these

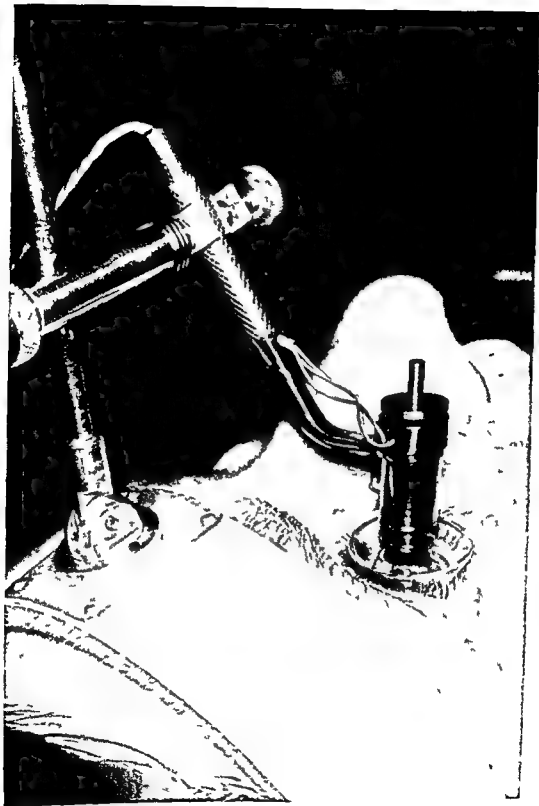


Fig 1

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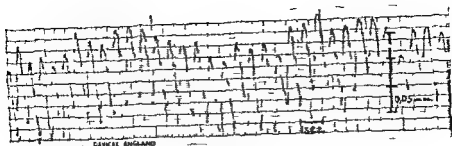


Fig 5
Exophthalmus pulsans

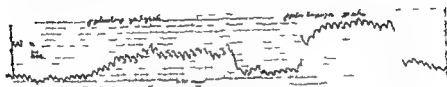


Fig 6
The effect of jugular vein compression

Summary

The pulsatory movements of the eyeball in the orbit are briefly described in normal cases and in exophthalmos pulsans. Some methods which have been used in the registration of the orbital pulsations are mentioned. A new method is described. An electronic Schiotz tonometer is fastened in relation to the head, so that the plunger, and only the plunger rests on a corneal contact lens. The tonometer is now used as a linear transducer. The pulsatory movements of the eyeball in the orbit are recorded as in tonography. Their size is found to be 2-3/100 mm in normal cases. Respiratory movements of about the same size are also frequently found. Increased and decreased pulsatory movements are registered in some pathological conditions.

REFERENCES

- Matt H J: Verbesserte Elektrotonographie mit einem Haltegerat. *Ophthalmologica* 1957 113: 134-139.
 Trol A: Ueber das graphische Registrieren der Vorwärts und Rückwärtsbewegungen des Auges. *Cracoe's Archiv für Ophthalm* 1901 52: 233-262.
 Hegner H: Neue Ergebnisse über die pulsatorischen Schwankungen des menschlichen Bulbus und seiner Hüllen. *Archiv für Augenheilk* 1930 102: 1-32.

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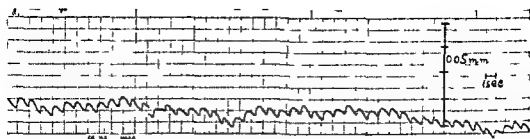


Fig 3
Normal orbital pulsations

cases the shape of the pulsations may be influenced both by the arterial and the venous pulse

Fig 5 shows a curve from a case of moderate exophthalmus pulsans caused by a highly vascularized orbital tumour. The pulsations have a magnitude of slightly less than $1/4$ mm, i.e. about 10 times the normal

In cases of orbital cellulitis the pulsations have been shown to be pathologically increased

In Fig 6 is demonstrated the effect of jugular vein compression. The resulted filling of the orbital veins brings the eye ball markedly forward

The approximate size of the variations of the blood volume in the orbit may be calculated from the registrations of the pulsatory movements of the eyeball. We then consider the eyeball together with the orbital septum as a piston in the orbit, $7 \text{ cm}^2 = 700 \text{ mm}^2$ in size. A movement of $1/100 \text{ mm}$ then corresponds to 7 mm^3 volume change of the orbital content. As the normal movements are $2-3/100 \text{ mm}$, we conclude that the normal pulse synchronous variations of the orbital blood volume are about $15-20 \text{ mm}^3$

The method described is recommended to be used as part of the diagnostic evaluation in cases of orbital diseases. The result of the registration may be of value in the differential diagnosis, and it may give information concerning the vascularization of an eventual orbital tumour. The method has the advantage that very little extra equipment is required. A tonograph, a holder for the tonometer, an eye speculum and a contact lens are all that is needed



Fig 4
Normal orbital pulsations atypical form

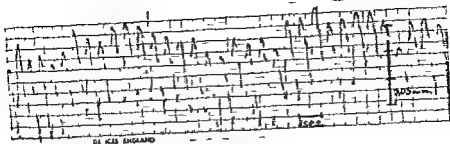


Fig 5
Exophthalmus pulsans

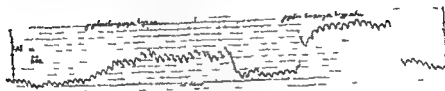


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The effect of jugular vein compression

Summary

The pulsatory movements of the eyeball in the orbit are briefly described, in normal cases and in exophthalmos pulsans. Some methods which have been used in the registration of the orbital pulsations are mentioned. A new method is described. An electronic Schiotz tonometer is fastened in relation to the head, so that the plunger and only the plunger rests on a corneal contact lens. The tonometer is now used as a linear transducer. The pulsatory movements of the eyeball in the orbit are recorded as in tonography. Their size is found to be 2-3/100 mm in normal cases. Respiratory movements of about the same size are also frequently found. Increased and decreased pulsatory movements are registered in some pathological conditions.

REFERENCES

- Matt H J: Verbesserte Elektrotonographie mit einem Haltegerät. *Ophthalmologica* 1957 133: 134-139.
- Tinl A: Ueber das graphische Registrieren der Vorwärts- und Rückwärtsbewegungen des Auges. *Gräfe's Archiv für Ophthalm.* 1901 52: 233-262.
- Hager H: Neue Ergebnisse über die pulsatorischen Schwankungen des menschlichen Bulbus und seiner Hüllen. *Archiv für Augenheilk.* 1930 107: 1-32.

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Copenhagen

OPHTHALMODYNAMOMETRY IN APOPLECTIC PATIENTS WITH HEMISPHERICAL INFARCTION OR TRANSITORY HEMISPHERICAL SYMPTOMS

By

Poul Kjer, M Eiken and F von Wouern

Interest in diagnosis of carotid artery disease has been considerable during the recent years. The reason may first of all be that in clinical as well as in autopsy materials an essential number of cases have been found with occlusion or stenosis of the internal carotid artery as the specific cause or contributing factor in cerebral vascular insufficiency. In large autopsy materials it has thus been demonstrated that stenosis or occlusion of the internal carotid artery occur in about 20 per cent of patients with cerebrovascular diseases⁷, and similar findings are reported in angiographic materials⁸. Next the increased interest in diagnosing carotid occlusion and stenosis may be found in the great development that has taken place during the last ten years in vascular surgery. New therapeutic methods have thus become possible and in suitable cases vascular surgery may be performed on the occluded or stenosed vessels of the neck in order to reestablish blood circulation or to remove the source of the emboli (¹ - ⁶). In this connection it is of great importance that about 40 per cent of the patients with permanent symptoms of hemispherical infarction before the vascular catastrophe have had transient episodes of neurological deficit from the same hemisphere or amaurosis fugax.

Clinically it is impossible to decide whether a cerebral infarction is caused by an occlusion of the internal carotid artery or the middle cerebral artery and it is practically impossible and also unreasonable to carry out arteriography on all patients with cerebral apoplexy. Using technically less difficult methods of examination it could be possible to select those patients for angiography who are suitable for vascular surgery. Theoretically ophthalmodynamometry (⁸ ¹ ¹⁶) or related methods as oculosphygmography (⁴ ⁵ ⁹) seem suitable as an introductory procedure being technically practicable and harmless in order to compare the haemodynamic conditions on the two sides. The drawback of the method

is that an occlusion of the internal carotid artery cannot be excluded if the pressure is the same on both sides as the collateral circulation can maintain a normal pressure in the retinal arteries on the same side as the carotid occlusion

Arteriography however should be performed on all patients who have only had transitory ischaemic attacks

Material and methods

Through a team work with all the departments at Gentofte Hospital we have attempted to do neurological examination and history to carry out arteriography, electroencephalography ophthalmodynamometry and carotid echography in all patients admitted to the hospital with symptoms of hemispherical infarction or transitory ischaemic attacks but with particular interest being paid to the patients with cerebro-vascular symptoms suggesting a disease in the arteries of the neck. No attempt of selection has been made and we have tried as much as possible to carry out the above mentioned examinations on all apoplectic patients referred to the hospital. Several patients however have not been registered either because they died before the examination programme could be carried through or on account of the general condition being too poor or other diseases giving contraindication to the examinations

All the patients (123 cases) had one or more arteriographies of the common carotid artery, on one or both sides and about one third of the cases (43 patients) had also aorto cervical arteriography by the method of Seldinger. In this examination a tube is introduced in the ascending aorta after punctuation of one of the big arteries of the extremities and contrast is injected through the tube. In this way the large neck arteries are reproduced in their full length from the arch of aorta to the base of the skull

The purpose of the present study was to correlate the results of arteriography with the results of ophthalmodynamometry and to draw attention to the value of ophthalmodynamometry in diagnosing carotid occlusion and stenosis. A pressure difference of 25 per cent or more between the two eyes was considered as a positive finding.

A preliminary report on the results of the examination in the first 42 patients has been published previously¹⁰. The complete study is not finished yet. The present material consists of a total of 123 patients, 104 of whom had hemispherical infarction and 19 only transitory ischaemic attacks (table 1). The distribution of age and sex is also seen in the table.

In the age group under 40 years there was a total of 7 patients (5 women and 2 men). 2 of the women (30 and 35 years old) with hemispherical infarction had taken oral contraceptives and arteriography

showed respectively occlusion of the middle cerebral artery and the internal carotid artery

A total of 67 patients had accompanying cardio vascular diseases (the numbers in brackets)

TABLE 1

THE PATIENT GROUP

AGE	FEMALE	MALE
<40	5(1)	2
40 - 49	2(2)	7(2)
50 - 59	10(2)	23(11)
60 - 69	15(12)	32(21)
>70	16(8)	11(8)
	48(25)	75(42)

HEMISPHERICAL INFARCTIONS 104

TRANSITORY ISCHEMIC ATTACKS

(HEMISPHERICAL) 19

TOTAL 123

Results

It has been connected with certain difficulties in finding a system for the results of angiography. In stenosis of the carotid artery for instance not only the degree and the extension of the stenosis have to be considered but also the degree of the atherosclerosis. In an attempt to compare the different findings schematic drawings have been made on the base of the X ray photographs and the angiographic findings have been divided as follows

- 1 Occlusion
- 2 Severe stenosis, i.e. the diameter of the stenosis is less than half of the diameter of the vessel before and after the stenosis
- 3 Moderate stenosis, i.e. a diameter larger than half of the diameter of the vessel
- 4 Severe atherosclerosis, i.e. a great length of the wall of the vessel is pronounced irregular and angiography does not show any real stenosis

TABLE 2
IMMEDIATE PROGNOSIS 104 COMPLETED STROKES

ANGIOGRAPHY	MODERATE CAROTID STENOSIS	SEVERE CAROTID STENOSIS	CAROTID OCCLUSION	MODERATE ATHERO-SCLEROSIS	SEVERE ATHERO-SCLEROSIS	HUNKING* STENOSIS OF INNOMINATE ARTERY	STENOSIS OF INTRACRANIAL PART	NORMAL	TOTAL
MEAN AGE	62	64	III	64	71	72	46	59	
DEAD		1	1				1	1	4
NO REMISSION	2	1	4	2	2			1	12
CONSIDERABLE REMISSION	4	5	10	4	1	2		11	37
TOTAL REMISSION	12	3	7	2	2			25	51
TOTAL	18	10	22	8	5	2	1	38	104

- 5 Moderate atherosclerosis
- 6 Hunking of the carotid artery
- 7 Normal conditions

Of course this angiographic classification can be criticised and it refers only to the conditions of the internal carotid artery, but not to its branches. Here it is necessary to draw attention to the fact that a total of 14 patients in the material had an occlusion of the middle cerebral artery. These 14 patients are equally dispersed in all the angiographic groups.

The prognosis for the patients with infarction of the hemisphere is of course very variable depending on the basic changes. Table 2 illustrates the clinical condition of the patients when discharged from the hospital correlated to age and the result of the angiography.

The prognosis is relatively better in the group where angiography showed normal conditions in the carotid artery.

One patient in this group died however and another had no remission of the paresis. Both patients had angiographically verified occlusion of the middle cerebral artery.

The clinical carotid symptoms: transitory ischaemic attacks, ipsilateral headache, bruits and the external carotid symptom are of limited diagnostic value (table 3).

The external carotid symptom is a visible prominence of one or more branches of the superficial temporal artery on the same side as the occluded internal carotid artery.¹¹ This symptom was only found in two cases.

Ophthalmodynamometry was carried out in 112 patients (table 4). A significant difference between the two sides was found in half of the

TABLE 3
CORRELATION OF ANGIOGRAPHY AND CLINICAL SIGNS AND SYMPTOMS

	NUMBER OF PATIENTS							
	20	16	24	11	4	4	2	42
ANGIOGRAPHY	MODERATE CAROTID STENOSIS	SEVERE CAROTID STENOSIS	CAROTID OCCLUSION	MODERATE ATHERO-SCLEROSIS	SEVERE ATHERO-SCLEROSIS	"KINKING" STENOSIS OF INNOMINATE ARTERY	STENOSIS OF INTRACRAN PART	NOR MAL
TRANSITORY ISCHEMIC ATTACKS	8	11	10	5	1	2	1	9
IPSILATERAL HEADACHE	1		2	3			1	1
BRUIITS	7	9	5	2	1		1	2
CAROTIS EXTERNA SYMPT			1					1

patients with severe stenosis and in about 2/3 of the patients with carotid occlusion

In a few cases with no significant difference between the two sides, remarkable low pressure values were found on both sides indicating a bilateral carotid obstruction

Finally it should also be mentioned that a few patients had positive ophthalmodynamometry and angiographically verified occlusion of both carotid arteries

In a total of 11 patients ophthalmodynamometry was not performed on account of diseases in one or both eyes retinal detachment, glaucoma

TABLE 4
CORRELATION OF ANGIOGRAPHY AND OPHTHALMODYNAMOMETRY

	NUMBER OF PATIENTS							
	20	16	24	11	4	4	2	42
ANGIOGRAPHY	MODERATE CAROTID STENOSIS	SEVERE CAROTID STENOSIS	CAROTID OCCLUSION	MODERATE ATHERO SCLEROSIS	SEVERE ATHERO SCLEROSIS	"KINKING" STENOSIS OF INNOMINATE ARTERY	STENOSIS OF INTRACRAN PART	NOR MAL
OPHTALMODY NAMOMETRY SIGN REDUCED IPSILAT. SIDE		8	15			1		2
SIGN REDUCED CONTRALAT SIDE								
INSIGNIFICANT	0	6	8	9	4	3	2	34
NOT DONE		2	1	2				6

TABLE 5
CORRELATION OF ANGIOGRAPHY AND OCULAR SYMPTOMS

ANGIOGRAPHY	NUMBER OF PATIENTS							
	20	15	24	11	4	4	2	42
	MODERATE CAROTID STENOSIS	SEVERE CAROTID STENOSIS	CAROTID OCCLUSION	MODERATE A. HERO SCLEROSIS	SEVERE A. HERO SCLEROSIS	"KINKING" STENOSIS OF INNOMINATE ARTERY	STENOSIS OF INTRACRAN. PART	NOR MAL
TRANSIENT MONOCULAR BUNDNESS	1	3	2			1		1(%)
OCCLUSION OF RETINAL ARTERY		1	2	1				
OCCLUSION OF RETINAL ARTERY WITH CONTRALAT. HOMONYMOUS HEMIANOPSIA		1						
HOMONYMOUS HEMIANOPSIA TRANSIENT PERMANENT				1 3		1		1 4
UNILATERAL RETINOPATHY	1	1	2					
PUPIL SMALLER ON AFFECTED SIDE		1		1				1
DIPLOPIA	1	2		1				1
UNEQUAL HYPERTENSIVE VASC. CHANGES		1						

with narrow angles cataract and recent embolus in the central retinal artery or its branches. Moreover poor cooperation made the examination impossible in a few cases.

Neuro-ophthalmological symptoms were found in 38 patients (table 5). Among the transitory ischemic symptoms special attention was paid to the monocular transient loss of vision (amaurosis fugax) which causes some patients to consult their ophthalmologist. This symptom however was only mentioned by 7 patients but it has probably been present in several more cases. Many of the patients however had aphasia were confused or unconscious on entering the hospital so that the case histories inevitably must be insufficient.

Occlusion of the central retinal artery was seen in 5 patients and angiography showed respectively severe stenosis occlusion and moderate atherosclerosis of the internal carotid artery. In one of these patients there was moreover contralateral homonymous hemianopsia.

Permanent homonymous hemianopsia was present in 20 patients while 2 patients only had transient hemianopsia. Many of these patients were

almost unable to cooperate at the examination on account of poor general condition. In four cases there was a sparing of the upper quadrant of the defective side of the field.

Unilateral retinopathy was seen in 4 patients. In this symptom cotton wool patches are seen in the nerve fiber layer of the eye homolateral to the lesion in the internal carotid artery¹⁴. As stated by Hollenhorst⁸ these patches are ischemic infarcts produced by hypotension.

This unilateral hypotension is probably also the reason for *asymmetric hypertensive retinal vascular changes with less hypertensive changes on the side of the affected carotid artery*¹⁰. This symptom was found in one case.

Afiosis on the affected side was seen in 3 patients and 5 complained of *diplopia*.

In addition to the symptoms mentioned in table 5, a few patients had respectively gaze palsy, conjugate deviation, unilateral ptosis, unilateral decreased corneal sensibility and unilateral paresis of the orbicularis oculi muscle.

14 patients had vascular surgery: Endarterectomy, removal of the thrombus or patch grafting. In 6 of these patients there was not 25 per cent difference in the pressure between the two eyes before surgery.

In 5 patients with more than 25 per cent difference between the eyes before surgery, the pressures became equal — at any rate in 4 of these patients after surgery. There was no follow-up examination of the fifth patient after surgery.

In 2 patients the difference between the two eyes was a little less than 25 per cent before surgery and no difference between the eyes after surgery.

Finally the examination could not be carried out in one patient.

Discussion and conclusion

In the present material consisting of 123 patients with permanent or transitory hemispherical symptoms hemiparesis was the most frequent symptom. This was present in 104 cases.

All the patients had one or more arteriographies, and in 24 cases occlusion of the internal carotid artery was found, while 16 cases showed severe carotid stenosis. 31 cases showed moderate changes of the internal carotid artery either as a slight stenosis (20 cases) or moderate atherosclerosis (11 cases). 4 patients had severe atherosclerosis and 6 patients showed various changes: kinking of the internal carotid artery, stenosis of the innominate artery or stenosis of the siphon.

42 patients showed normal conditions of the internal carotid artery.

The usual clinical symptoms including the neuro ophthalmological carotid symptoms were only of limited value in diagnosing an obstruction of the internal carotid artery.

Hollenhorst⁶ has stated that the incidence of amaurosis fugax is higher among patients having intermittent insufficiency than among those having thrombosis. This is confirmed in the present series but the number of patients with this symptom is rather limited.

Regarding the homonymous hemianopsia Walsh¹⁵ has pointed out that often there is a relative sparing of the upper quadrant of the defective side of the field. This is ascribed to the fact that the superior portion of the optic radiations is supplied by the middle cerebral artery and the lower portion by the posterior cerebral artery. In the present material 4 patients had a lower homonymous quadrantanopsia. The angiographic findings in these 4 patients were respectively, occlusion, severe stenosis and atherosclerosis of the internal carotid artery.

As an exact diagnosis is of vital importance for a possible treatment and for the study of the spontaneous course of the cerebrovascular diseases it is obvious that there has been great interest in finding other and simpler methods of examination than arteriography.

Ophthalmodynamometry has proved to be useful in a number of cases and in the present material there was positive finding in about half of the cases with severe stenosis and about 2/3 of the cases with occlusion of the internal carotid artery.

Weigelin and Lobstein¹⁶ found reduced pressure in 70-80 per cent of the cases with unilateral carotid occlusion.

In the present examination a pressure difference of 25 per cent between the two eyes was considered significant (according to Spalter), but other authors (^{17, 18}) have considered a difference less than 25 per cent as significant.

Ophthalmodynamometry does not render arteriography superfluous, as the moderate stenoses or mural thrombi do not change the haemodynamic conditions to such a degree that they possibly could be disclosed by ophthalmodynamometry. The method however is suitable as the first examination in obscure cerebral insults, amaurosis fugax, unilateral retinopathy, hemianopsia and the like.

Furthermore a positive ophthalmodynamometry compared with a negative common carotid arteriography indicates the performance of the more comprehensive central arteriography in cases felt to be suitable for surgery.

Considering the great interest in diagnosing the cerebrovascular diseases and the increasing therapeutic activity, ophthalmodynamometry may in our opinion contribute in essential respects — also to the post-operative follow up of the effect of vascular surgery.

almost unable to cooperate at the examination on account of poor general condition. In four cases there was a sparing of the upper quadrant of the defective side of the field.

Unilateral retinopathy was seen in 4 patients. In this symptom cotton wool patches are seen in the nerve fiber layer of the eye homolateral to the lesion in the internal carotid artery¹⁴. As stated by Hollenhorst³ these patches are ischemic infarcts produced by hypotension.

This unilateral hypotension is probably also the reason for *asymmetric hypertensive retinal vascular changes* with less hypertensive changes on the side of the affected carotid artery¹⁰. This symptom was found in one case.

Miosis on the affected side was seen in 3 patients and 5 complained of *diplopia*.

In addition to the symptoms mentioned in table 5, a few patients had respectively gaze palsy, conjugate deviation, unilateral ptosis, unilateral decreased corneal sensibility and unilateral paresis of the orbicularis oculi muscle.

14 patients had vascular surgery (Endarterectomy, removal of the thrombus or patch grafting). In 6 of these patients there was not 25 per cent difference in the pressure between the two eyes before surgery.

In 5 patients with more than 25 per cent difference between the eyes before surgery, the pressures became equal — at any rate in 4 of these patients after surgery. There was no follow up examination of the fifth patient after surgery.

In 2 patients the difference between the two eyes was a little less than 25 per cent before surgery and no difference between the eyes after surgery.

Finally the examination could not be carried out in one patient.

Discussion and conclusion

In the present material consisting of 123 patients with permanent or transitory hemispherical symptoms hemiparesis was the most frequent symptom. This was present in 104 cases.

All the patients had one or more arteriographies, and in 24 cases occlusion of the internal carotid artery was found, while 16 cases showed severe carotid stenosis. 31 cases showed moderate changes of the internal carotid artery either as a slight stenosis (20 cases) or moderate atherosclerosis (11 cases). 4 patients had severe atherosclerosis and 6 patients showed various changes: kinking of the internal carotid artery, stenosis of the innominate artery or stenosis of the siphon.

42 patients showed normal conditions of the internal carotid artery.

The usual clinical symptoms including the neuro ophthalmological carotid symptoms were only of limited value in diagnosing an obstruction of the internal carotid artery.

Hollenhorst⁸ has stated that the incidence of amaurosis fugax is higher among patients having intermittent insufficiency than among those having thrombosis. This is confirmed in the present series but the number of patients with this symptom is rather limited.

Regarding the homonymous hemianopsia Walsh¹⁵ has pointed out that often there is a relative sparing of the upper quadrant of the defective side of the field. This is ascribed to the fact that the superior portion of the optic radiations is supplied by the middle cerebral artery and the lower portion by the posterior cerebral artery. In the present material 4 patients had a lower homonymous quadrantanopsia. The angiographic findings in these 4 patients were respectively occlusion, severe stenosis and atherosclerosis of the internal carotid artery.

As an exact diagnosis is of vital importance for a possible treatment and for the study of the spontaneous course of the cerebrovascular diseases, it is obvious that there has been great interest in finding other and simpler methods of examination than arteriography.

Ophthalmodynamometry has proved to be useful in a number of cases and in the present material there was positive finding in about half of the cases with severe stenosis and about 2/3 of the cases with occlusion of the internal carotid artery.

Weigelin and Lobstein¹⁶ found reduced pressure in 70–80 per cent of the cases with unilateral carotid occlusion.

In the present examination a pressure difference of 25 per cent between the two eyes was considered significant (according to Spilster) but other authors (^{17, 18}) have considered a difference less than 25 per cent as significant.

Ophthalmodynamometry does not render arteriography superfluous as the moderate stenoses or mural thrombi do not change the haemodynamic conditions to such a degree that they possibly could be disclosed by ophthalmodynamometry. The method however is suitable as the first examination in obscure cerebral insults, amaurosis fugax, unilateral retinopathy, hemianopsia and the like.

Furthermore a positive ophthalmodynamometry compared with a negative common carotid arteriography indicates the performance of the more comprehensive central arteriography in cases felt to be suitable for surgery.

Considering the great interest in diagnosing the cerebrovascular diseases and the increasing therapeutic activity, ophthalmodynamometry may in our opinion contribute in essential respects — also to the post-operative follow up of the effect of vascular surgery.

Summary

The results of ophthalmodynamometry and carotid angiography are compared in 123 apoplectic patients with hemispherical infarction or transitory hemispherical symptoms

Ophthalmodynamometry showed a significant difference between the two sides in half of the patients with severe stenosis of the carotid artery and in about 2/3 of the patients with carotid occlusion. The clinical carotid symptoms and especially the neuro ophthalmological symptoms are compared with the results of angiography

14 patients had vascular surgery. An account is given of the result of ophthalmodynamometry in these cases

REFERENCES

- 1 Bertelsen, S., Mathiesen, F. R., Poulsen, D. Thue and Ohlenschläger, H. H. *Ugeskr Læg* 1968 130 542
- 2 Boysen, G., Engell, H. C. and Lauridsen, P. *Nord Med* 1968 79 582
- 3 Bull, J. W. D., Marshall, J. and Shaw, D. A. *Lancet* 1960 1 562
- 4 Bynke, H. G. *Neurology* 1966 16 383
- 5 Bynke, H. G. *Acta Ophthal* 1968 46 792
- 6 Engell, H. C. *Nord Med* 1968 79 69
- 7 Fischer, C. M. *Arch Neurol Psychiat (Chic)* 1954 72 346
- 8 Hollenhorst, R. W. *Amer J Ophthal* 1959 47 753
- 9 Jensen, S. *Acta Ophthal* 1968 46 674
- 10 Lørbj, T. J. Jr and Hollenhorst, R. W. XVII Concilium Ophthalmologicum Acta (1954) 1955 1 335
- 11 Olavius, B. de Fine. *Acta Neurol Scandinav* 1965 41 539
- 12 Spalter, H. F. *Amer J Ophthal* 1959 47 453
- 13 Suen, H. J. and Hollenhorst, R. W. *Proc Staff Meet Mayo Clin* 1956 31 684
- 14 Swan, A. C. and Raaf, J. *Tr Am Ophth Soc* 1951 49 435
- 15 Walsh, F. B. *Clinical Neuro ophthalmology* 1957 Baltimore Williams and Wilkins 2 ed pp 791-802
- 16 Weigelin, E. and Lobstein, A. *Ophthalmodynamometry* 1963 Basel and New York, S. Karger 134 pp
- 17 Wood, F. A. and Toole, J. F. *JAMA* 1957 165 1264
- 18 Wouern, F., Eiken, M., Hansen, O. E., Jørgensen, O. E., Kjær, P., Kristensen, J. A. and Mortensen, T. *Danish Med Bull* 1968 15 218

Discussion

I. Horien (Oslo)

At the Neurosurgical department in Rikshospitalet, Oslo, we have had the opportunity to carry out dynamic tonometry when the internal carotid artery was ligated in cases with intracranial aneurisms. It was possible to observe the development of collateral circulations from the ipsilateral external carotid artery and from the contralateral internal carotid artery. It starts a few hours after the obliteration.

In some cases the collateral circulation can be of such a magnitude that tests done months or years afterwards fail to show any differences in the amplitude of the cornea pulsation on the two sides. In such long standing cases the dynamic tonometry combined with a compression manoeuvre of the carotid artery may give valuable diagnostic informations.

We do agree with dr Bynke to abstain from compression of the carotid artery in acute cases of artery occlusions or stenosis which has resulted in cerebral insults. An indiscriminate use of the compression method might endanger the patient by dislodging an arterial thrombus. The acute cases will usually produce a significant difference in the cornea pulsations as measured by dynamic tonometry. This will make the compression manoeuvre superfluous.

From Oslo University Eye Department, Rikshospitalet Oslo, Norway
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DYNAMIC TONOMETRY

IV The corneal indentation pulse in giant cell arteritis

By

Ivar Horven

Patients suffering from giant cell arteritis may clinically be divided into three groups, those with no eye involvement, which means approximately 50–60 per cent of the cases (*Egge et al 1966, Meadows 1968*), those with symptoms from one eye, and those with symptoms from both eyes. The need has been pressing for a safe clinical test by which the immediate danger of eye involvement could be evaluated in these cases. This test should be sensitive enough to give a conclusive answer in eyes with a minor decrease in blood supply, a decrease which up to testing time not yet had caused any clinical symptoms.

The purpose of the present study is to present dynamic tonometry (*Horven 1968*) as an easy, accurate and safe clinical test in these cases. A test which offers information of diagnostic and, sometimes, of prognostic interest.

Material and methods

The study includes all cases of giant cell arteritis which were treated for eye involvement in our department during the period November 1967–May 1969. Case no. 1 was examined with a provisory set up in January 1967 and is also included in the present material. There were 10 patients, 8 males and 2 females. The age averaged 72.1 years (57–80) and the erythrocyte sedimentation rate (SR) at admittance was elevated in all cases with an average value of 65.3 mm per hour (40–98). Histological examination of a temporal artery biopsy yielded pathological findings typical for giant cell arteritis in all but one of the cases studied, in this one case (Case no. 10) no giant cells were found although definite pathological changes were demonstrated in the intima and media of the artery wall including partial disappearance of the internal elastic lamella.

Dynamic tonometry was performed at admittance and at various intervals during the period of treatment of the patients in question. Due

to summer vacation Case no 6 had the initial dynamic tonometry examination postponed to 11 days following start of treatment. The dynamic tonometer is made according to the known principles of electronic tonometers with certain important modifications (Horten 1968). In its present state the tonometer yields an output of 1 mV per 1μ plunger deflection. An output of 50 mV will, therefore, correspond to a plunger movement of 50μ which equals one scale reading Schiotz. When high sensitivity is employed, the tracings may be kept on the running paper of the recorder by use of a zero suppression unit.

The corneal indentation pulse amplitudes as recorded with the dynamic tonometer is normally of the same order of magnitude in the two eyes with an average value of about 30μ of plunger movement which equals 0.6 scale reading Schiotz. Based on statistical evaluations of the results obtained in 65 subjects the difference in amplitude between the two eyes of the same subject is normally less than 15 per cent (Horten 1970). Thus a pathological result of this test in patients suffering from giant cell arteritis may be defined as follows: 1. By demonstration of a decrease in corneal indentation pulse amplitudes of 15 per cent or more in eyes yielding clinical symptoms of the disease. 2. By recording corneal indentation pulse amplitudes of less than 13μ in eyes with or without clinical symptoms. A 13μ corneal pulse amplitude is the lowest value ever recorded in a normal eye (Horten 1970).

Results

The results obtained are summarized in Table 1.

A marked decrease in corneal indentation pulse amplitudes was demonstrated in all but one (Case no 6) of the eyes yielding clinical symptoms of giant cell arteritis. In the 8 eyes which demonstrated a visual acuity of light perception (1p) or amaurosis at admittance the corneal pulse amplitudes averaged 2.6μ (0-12). As a rule the decrease in corneal pulse amplitude was more pronounced in the amaurotic eyes although a zero pulse amplitude was recorded in an eye with 5/7.5 in visual acuity (Case no 7).

In Case no 6 a 13 per cent decrease (normal eye 60μ affected eye 52μ decrease 8μ) was demonstrated in the affected eye. This decrease is regarded as a possible but not definite pathological finding. As mentioned above the initial dynamic tonometry test was performed 11 days following start of treatment in this case which possibly explains why only a minor difference was found.

Of the 10 cases studied 3 yielded bilateral symptoms at admittance in hospital. 7 offered definite pathological dynamic tonometry test results in both eyes and 1 a possible pathological test result in the mate eye.

Table 1
Results obtained in 10 patients suffering from giant cell arteritis
fc = finger counting Lp = light perception, am = amaurosis

Case no	Initial corneal pulse amplitude (μ)		No of eyes with clinical symptoms	No of eyes with positive test result	Initial		Visual acuity		Final		Follow up period
	Right	Left			Right	Left	Right	Left	Right	Left	
1	2	2	2	2	1 mfc	am	6 mfc	am	5/7	5	28 months
2	0	2	1	2	am	5/10	am	5/7	5	10	"
3	20	12	1	1+	5/10	1 mfc	5/10	5/7	5	15	"
4	17	37	1	1	2 mfc	5/5	2 mfc	5/5		17	"
5	11	12	2	2	5/30	am	3 mfc	am		6	"
6	60	52	1	2	5/5	5/25	5/5	5/7	5	10	"
7	1	0	1	2	1 p	5/7	am	5/5		2	"
8	10	0	1	2	5/5	1 p	5/5	am		2	"
9	0	0	2	2	am	am	am	am		1 week	"
10	12	6	1	2	5/10	am	5/10	am		1	"

? = see text

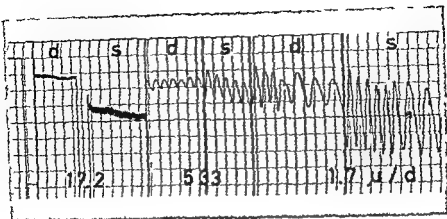


Fig 1

leaving only 2 patients (i.e. 20 per cent) with monolateral eye involvement. This points to a marked tendency of bilateral eye involvement which stresses the importance of immediate action what concerns therapy of these patients.

In the following some of the cases will be briefly mentioned and commented.

Case no. 4 is an example of monolateral eye involvement in a man aged 57. He was admitted with a visual acuity of finger counting (f.c.) 2 m on the right (d) eye which yielded a decrease in corneal pulse amplitudes to 46 per cent of the normal mate eye values as shown in Fig. 1. The amplitudes of the mate eye was normally sized which indicated that there was no imminent danger of involvement of this normal mate eye. One year later his left subclavian artery was partially occluded possibly because of a giant cell arteritis lesion at this site.

Case no. 1 (male aged 71) was admitted in January 1967 with bilateral symptoms and a visual acuity of 1 m f.c. in right eye and amaurosis in the left. With a provisory set up the corneal pulse amplitudes were measured to equal 2μ in both eyes. One year later the amplitudes were normal in magnitude and the vision was 6 m f.c. in right eye and amaurosis in left eye. This demonstrates the fact that following adequate therapy the occluded artery may re-canalize with increase in blood supply and what is important with increase in vision in the eye which initially yielded a visual acuity of finger counting II, however the eye is amaurotic or yields only light perception when treatment is started we have never experienced any increase in function although the corneal pulse amplitudes may rise to sub normal or normal levels.

Case no. 2 (male aged 76) had suffered from diplopia of one week duration when he suddenly became amaurotic on the right eye. Initially

he suffered no symptoms from the left eye which yielded a visual acuity of 5/10, although the dynamic tonometry test demonstrated a bilateral involvement of ocular blood supply (see Table 1) One month later following treatment and still on steroids he got an attack of leftsided amaurosis fugax of 5 minutes duration Four months later, still on steroids and with a normal SR of 11 mm per hour he wakened from his afternoon nap amaurotic on both eyes The vision on left eye was completely gone for 2 hours but returned afterwards to 5/7 5 In comment to this observation the blindness in Case no 10 (female, aged 77) was also first noticed on waking

Case no 3 (male, aged 66) suffered from symptoms in the left eye of four days duration when he was admitted in our department in March 1968 His left fundus demonstrated ischemic changes with exception of the part nourished from a cilioretinal artery, his right fundus was normal The visual acuity was 5/10 on the right side, 1 m f c on the left The corneal pulse amplitude measured $20\ \mu$ in the right eye, which is in the lower normal range and made us suspect a slight involvement also in the right ophthalmic artery in spite of the normal fundus picture On the left side the amplitudes were $12\ \mu$ which is a definite decrease, as shown in Fig 2 Steroids had good effect on the SR, the corneal pulse amplitudes continued, however, to decrease on the left side Our suspicion concerning right eye involvement turned out to be valid, the sixth day his vision on right eye fell to 5/50 and ischemic lesions were demonstrated in his right eye fundus Treatment was increased including Rheomakrodex infusions and two months later his vision was 5/10 in both eyes The follow up period was complicated with several attacks of broncho pneumonia Half a year later he suddenly got a new attack of his giant cell arteritis, with zero corneal pulse amplitudes and reduction of visual acuity to 5/15 — in both eyes The treatment was once again increased and vision improved to 5/10 on right side and 5/7 5 on the left side where his cilioretinal artery

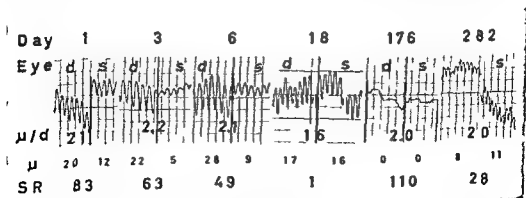


Fig 2

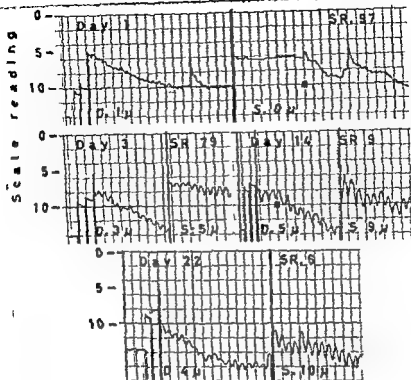


Fig 3

was still functioning. At the latest control on day 452 the corneal pulse amplitudes measured 15 and 16 μ in the respective right and left eye.

Case no. 7 (male aged 76) yielded 1 p on right eye with no symptoms from his left eye which demonstrated a visual acuity of 5/7.5. The dynamic tonometry test results are presented in Fig. 3. A bilateral involvement of ocular blood supply was found. The following day an ischemic lesion at the disc margin was noted in the left eye. Treatment yielded excellent results with no reduction in vision of this left eye.

Case no. 11 (female aged 68) yielded 1 p on left (s) eye with no symptoms from the right eye at admittance in our department. The dynamic tonometry test yielded, however, decreased corneal pulse amplitudes in both eyes demonstrating a bilateral involvement as shown in Fig. 4. The corneal pulse amplitudes increased on both sides following treatment, which indicates that this test may offer valuable information also concerning the effect of treatment.

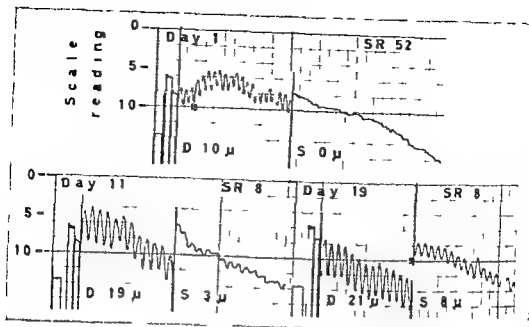


Fig 4

Comment

The ocular blood flow consists of two parameters, the non pulsatile flow which is equal in size through the total heart cycle, and the pulsatile flow which enters the eye in systole. The excess of blood which enters the eye in systole because of this pulsatile flow initiates a pulsesynchronous change in intraocular pressure which may be recorded by use of dynamic tonometry. If a decrease in ocular blood supply exists, as in internal carotid artery occlusion, a corresponding decrease may be noted in the corneal indentation pulse amplitudes (Castren & Laishanen 1964, Bynke 1966, Bron *et al* 1967, Galin 1967). A decrease in intraocular pulsation have also been demonstrated in luetic choroidal atrophy (Suzuki 1962) and in our department by tapetoretinal degenerations. In central retinal artery embolism only a minor, 10 per cent decrease exists in the intraocular pulsation (Thiel 1928, Suzuki 1962), probably because of normal choroidal blood supply of these eyes. This important fact was also confirmed by dynamic tonometry test results obtained in 4 fresh and typical cases of central retinal artery embolism in our department. Accordingly, this test may be helpful in order to differentiate between central retinal artery embolism and giant cell arteritis, two diseases which may yield identical ophthalmoscopical findings.

In the present study a marked decrease in corneal pulse amplitudes was demonstrated in eyes suffering from giant cell arteritis, which strongly suggests that a corresponding decrease exists in both retinal and choroidal blood supply in these cases. The zero pulse amplitude recorded

in Case no 7 in the one eye with a visual acuity of 5/7 5 indicates that the pulsatile flow may be stopped completely while the eye still receives sufficient nourishment from the remaining non pulsatile flow

Meadows (1968) stresses the point that the onset of blindness in giant cell arteritis is usually abrupt and often first noticed on waking, an observation which is confirmed by Case no 2 and Case no 10 in the present study McGowan (1967) reports a case of giant cell arteritis which was amaurotic in one eye and developed amaurosis in the other eye following general anesthesia A similar case was recently observed in Oslo City Hospital (Bergaust 1968) in this case the diagnosis of giant cell arteritis was verified after general anesthesia was given with amaurosis as a result Most probably these eyes which yielded no symptoms prior to general anesthesia still had a reduced ocular blood supply as a consequence of giant cell arteritis lesions in their ophthalmic arteries This possibility has been proved valid in some of the cases presented in the present study The above observations may be explained by the fact that a marked decrease in corneal pulse amplitudes is also initiated by sleep following Seconal (mchallymal) or Thiopentone (thiomebumal) administration and during ether or Halothane general anesthesia (Horten & Sjørdalen 1970) When this anesthesia effect comes in addition to the reduction in ocular blood supply induced by the giant cell arteritis, a further decrease in corneal pulse amplitudes and ocular blood supply may be initiated with amaurosis as a result As a consequence of this interpretation it is advisable for patients suffering from giant cell arteritis to have a dynamic tonometry test performed prior to accepting surgery under general anesthesia If this test demonstrates a decrease in corneal pulse amplitudes in eyes with useful vision, the general anesthesia should if possible be postponed

Summary

Dynamic tonometry have been performed in 10 patients suffering from giant cell arteritis Seven of the patients complained of symptoms in one eye and three in both eyes at admittance in our department The dynamic tonometry test demonstrated however, a bilateral involvement of the ocular blood supply in 8 of the patients Thus dynamic tonometry is regarded as a sensitive accurate and safe clinical test which offers results of diagnostic and prognostic importance in these patients Moreover, the test offers a unique opportunity to differentiate patients suffering from giant cell arteritis from central retinal artery embolism as the latter group of patients yield normal or close to normal corneal pulse amplitude values even when the eye is amaurotic

REFERENCES

- Bron, A J, Knox, D L and Gaasterland, D Tonographic studies in carotid occlusive disease, *Brit J Ophthal* 51 577-595, 1967
- Bynke, H G Screening diagnosis of carotid occlusion by means of oculosphygmography, *Neurol* 16 383-391, 1966
- Castren, J A and Laikainen, P New method of diagnosing carotid diseases, *Acta Ophthal (Kbh)* 42 219-223 1964
- Egge, A, Midtbo A and Westby R Arteritis temporalis *Acta Ophthal (Kbh)* 44 49-56, 1966
- Galin H G, Rodriguez Barrios R, Pola R and Mclean, J M Cerebrovascular insufficiency, *Trans Amer Acad Ophthal Otolary* 71 119-125, 1967
- Horten, I Dynamic tonometry I The dynamic tonometer, *Acta Ophthal (Kbh)* 46 1213-1221, 1968
- Horten I Dynamic tonometry III The corneal indentation pulse in normal and glaucomatous eyes *Acta Ophthal (Kbh)*, 48 39-58, 1970
- Horten, I and Syrdalen P Corneal indentation pulse and general anesthesia *Acta Ophthal (Kbh)*, 48 59-66 1970
- McGowan, B L Active temporal arteritis as a contraindication to elective surgery with general anesthesia, *Amer J Ophthal* 64 455-457, 1967
- Meadows S P Temporal or giant cell arteritis — ophthalmic aspects, Chapter 10 pp 148-157 in L Lawton Smith *Neuro ophthalmology* Vol IV C V Mosby C, Saint Louis 1968
- Thiel R Hornhautpulsation Blutdruck und Augendruck *Klin Mbl Augenheilk* 81 353, 1928
- Suzuki I Corneal pulsation and corneal pulse waves *Jap J Ophthal* 6 190-194 1962

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CORNEAL INDENTATION PULSE AND RETROBULBAR ANESTHESIA

By

Per Syrdalen and Ivar Horven

During general anesthesia a striking decrease in corneal indentation pulse amplitudes have been demonstrated by use of dynamic tonometry (Horven & Syrdalen 1970). This decrease in amplitudes is probably reflecting a corresponding decrease in ocular blood supply, which may explain why general anesthesia may initiate disastrous results in patients suffering from giant cell arteritis (McGowan 1967).

The present investigation was performed in order to study if a similar change in corneal indentation pulse amplitudes might be initiated by retrobulbar anesthesia. If so, the study should offer information whether the decrease in amplitude was caused by the anestheticum itself, the adrenalin (Exadrin) or the vehicle injected.

Material

The material consists of 67 patients with the following disorders: Various forms of glaucoma 32, retinal detachment 21, choroidal melanoma 12, strabismus 2. There were 23 males and 44 females and the age averaged 61.8 years (24-83).

The material was divided at random in the following groups based upon the drug injected:

- A. Nylocain Exadrin 1%† 20 patients: 3 males and 17 females. Average age 63.9 years (29-83). (Retinal detachment 10, glaucoma 7, strabismus 2, choroidal melanoma 1).
- B. Nylocain Exadrin 2%† 20 patients: 7 males and 13 females. Average age 58.7 years (24-81). (Choroidal melanoma 7, retinal detachment 7, glaucoma 6).

† Nylocain Exadrin 1 resp 2 contains lidocain chloride 10 mg resp 20 mg and adrenalin 0.01 mg resp 0.0125 mg per ml. Exadrin contains adrenalin 0.0125 mg per ml and was kindly supported by A/B Astra Sweden.

- C Xylocain 1% 20 patients, 9 males and 11 females Average age 63.1 years (35-77) (Glaucoma 15, retinal detachment 4, choroidal melanoma 1)
- D Xylocain 2% 1 female patient aged 45 (Glaucoma)
- E Exadrin† 3 males with an average age of 75 (70-80) (Glaucoma absolutum 3)
- F Saline 0.9% 3 patients, 1 male and 2 females Average age 52.3 years (44-60) (Choroidal melanoma 3)

Only groups A, B and C consist of a fair number of patients, they are not, however, directly comparable as Group C is over represented with glaucoma patients

Group D consists of only one patient. The second patient we gave Xylocain 2% developed a severe side reaction with loss of consciousness and fall in arterial blood pressure. The cause of this side reaction was probably leakage of the anestheticum into the optic nerve sheaths and into the cranial cavity. This reaction subsided completely in a couple of hours without leaving any traces. Due to this side reaction we did not use Xylocain 2% without adrenalin to other patients.

The three patients in Group E which initially received Exadrin were afterwards given Xylocain 2% with a percentage reduction in corneal indentation pulse amplitude of a similar order of magnitude as seen in the patient of Group D (see also Table II).

A retrobulbar injection of Exadrin or Saline followed by a second injection of anestheticum was restricted to patients with eyes which were to be removed. A limitation of available cases existed which explains why Group E and Group F only consist of three patients each. By chance Group E happened to consist of hypertensive glaucomatous eyes and Group F of hypotensive choroidal melanoma eyes (Dunnington 1938, Horven 1969).

Methods

On the day of surgery dynamic tonometry (Horven 1968) was performed under topical anesthesia (oxibuprocain). Immediately afterwards a retrobulbar injection of 4.5 ml was given, as specified for the various groups listed above. A second dynamic tonometry was performed 10 minutes after the retrobulbar injection.

The eye tension was measured in scale reading Schiotz and converted into mm Hg intraocular pressure (P_0) by use of Friedenwald's 1955 converting table. In Group A the eye tension was measured with the 5.5 and 10 g plunger weight in order to evaluate the scleral rigidity by use of Friedenwald's 1955 nomogram.

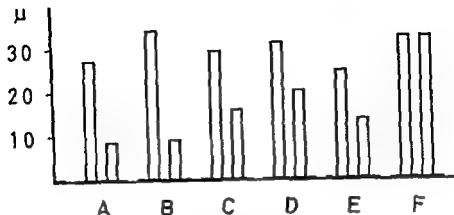


Fig 1

Average corneal indentation pulse amplitude in μ before and after retrobulbar injection in the various groups of patients

The corneal indentation pulse amplitudes were recorded in microns of plunger movement (μ) and converted into mm^3 change in ocular volume (ΔV) by use of the converting table based on Langham-Hetland-Eriksen's data as previously described (Hovnen 1970a)

Visual acuity was recorded before and 8 minutes after injection in all cases of Group C

The statistical method of paired comparison was applied to the data obtained before and after injection within the groups. When the various groups were compared with each other, the Student's *t* test was applied. The statistical significance levels are indicated as follows: * = significant at the 5% level; ** = significant at the 1% level; *** = significant at the 0.1% level.

Results

The results obtained are specified as to change in corneal indentation pulse amplitudes (μ), ocular volume (ΔV) and intraocular pressure (mm Hg) as shown in Table I. Figure 1 visualizes the change in μ obtained in the various groups of patients.

Saline No significant change in μ , ΔV or mm Hg was obtained in Group F. Most probably, therefore, the vehicle itself is not responsible for the changes presented below. A typical recording is shown in Figure 2.

Exadrin A significant (*) decrease in μ and ΔV was obtained following retrobulbar injection of Exadrin (Group E) with an average reduction to 54% and 52.2% respectively, of the value obtained before injection. A minor and not significant decrease to 87% was observed in mm Hg intraocular pressure (Table I).

- C Xylocain 1% 20 patients, 9 males and 11 females Average age 63.1 years (35-77) (Glaucoma 15, retinal detachment 4, choroidal melanoma 1)
- D Xylocain 2% 1 female patient aged 45 (Glaucoma)
- E Exadrin† 3 males with an average age of 75 (70-80) (Glaucoma absolutum 3)
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The three patients in Group E which initially received Exadrin were afterwards given Xylocain 2% with a percentage reduction in corneal indentation pulse amplitude of a similar order of magnitude as seen in the patient of Group D (see also Table II).

A retrobulbar injection of Exadrin or Saline followed by a second injection of anestheticum was restricted to patients with eyes which were to be removed. A limitation of available cases existed which explains why Group E and Group F only consist of three patients each. By chance Group E happened to consist of hypertensive glaucomatous eyes and Group F of hypotensive choroidal melanoma eyes (Dunnington 1938, Hørvén 1969).

Methods

On the day of surgery dynamic tonometry (Hørvén 1968) was performed under topical anesthesia (oxibuprocain). Immediately afterwards a retrobulbar injection of 4.5 ml was given, as specified for the various groups listed above. A second dynamic tonometry was performed 10 minutes after the retrobulbar injection.

The eye tension was measured in scale reading Schiotz and converted into mm Hg intraocular pressure (P_0) by use of Friedenwald's 1955 converting table. In Group A the eye tension was measured with the 5.5 and 10 g plunger weight in order to evaluate the scleral rigidity by use of Friedenwald's 1955 nomogram.

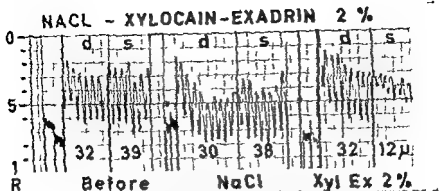


Fig 2

no decrease in corneal indentation pulse amplitudes following left side retrobulbar injection of saline. Decrease of corneal indentation pulse amplitudes following injection of Xyllocain Exadrin. d=right eye s=left eye

Xyllocain The anestheticum was injected in two concentrations 1% (Group C) and 2% (Group D and Group E). In Group E the patients had on beforehand received a retrobulbar injection of Exadrin as previously described. The results from this Group E is given in Table II. An average reduction in μ to 53.3% (Group C) 64.3% (Group D) and 57.5% (Group E) was obtained. Typical recordings from Group C and Group D are presented in Figure 3 and Figure 4.

Table II
Results obtained by retrobulbar injection of Exadrin
followed by Xyllocain 2%

	Exadrin		Xyllocain 2%	
	Before	After	Before	After
μ (average)	24.67	13.33	13.33	7.67
σ (of pop.)	10.26	7.09	7.09	3.21
$\% \left(\frac{\text{After}}{\text{Before}} \cdot 100 \right)$		40		57.5
t value/ sign level	1107*		2.125	

The results indicate that there is *no* difference in corneal indentation pulse amplitude reducing effect by 1% or 2% Xyllocain both concentrations yielding a reduction in μ to about 50-60% of the value obtained before injection. This indication is offered with the reservation that the groups are not directly comparable only Group C consists of a fair number of patients. In this Group C (Xyllocain 1%) there was a highly

Table I

Dynamic tonometry results (average) in the various groups of patients. The statistical method of paired comparison is applied to the results obtained before and after retrobulbar injection

Significance levels * = 5% ** = 1%, *** = 0.1%

	Group A Xyl Exadr 1%		Group B Xyl Exadr 2%		Group C Xyl 1%		Group D Xyl 2%		Group E Exadrin		Group F Saline	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
N	20	20	20	20	20	20	1	1	3	3	3	3
μ (average)	27.15	8.40	33.95	8.90	29.35	15.65	31.00	20.00	24.67	13.33	32.33	32.33
σ (of pop.)	13.11	7.26	11.46	4.69	10.14	8.66			10.26	7.09	9.07	8.14
% $\left(\frac{\text{After 100}}{\text{Before}}\right)$	30.9		26.2		53.3		64.5		54.0		100	
t value/sign level	10.669***		10.857***		10.559***				6.107*			
ΔV (average)	2.84	0.87	3.41	0.91	3.26	1.68	3.50	2.60	2.95	1.54	3.17	3.13
σ (of pop.)	1.86	0.88	1.33	0.47	1.30	1.23			1.31	0.82	0.94	0.82
% $\left(\frac{\text{After 100}}{\text{Before}}\right)$	30.8		26.7		51.6		74.3		52.2		98.7	
t value/sign level	7.937***		10.264***		7.668***				4.978*		0.115	
I_0 (average)	14.95	13.08	17.33	13.56	29.11	21.41	24.40	31.60	76.60	66.67	8.43	9.50
σ (of pop.)	7.29	6.42	12.58	11.00	19.24	13.41			22.07	13.11	4.79	4.29
% $\left(\frac{\text{After 100}}{\text{Before}}\right)$	87.5		78.2		73.5		129.3		87.0		112.7	
t value/sign level	2.747*		2.700*		2.692*				1.753		1.031	

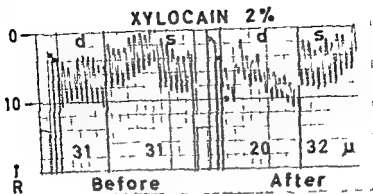


Fig 4

Decrease in corneal indentation pulse amplitudes following right side retrobulbar injection of Xylocain 2%

significant (***) decrease both in μ and ΔV with an average reduction to 53.3% and 51.6%, respectively, of the value obtained before injection. A significant (*) decrease to 73.5% was also noted in mm Hg intraocular pressure. However, Group C contained a fairly high number of glaucoma patients with increased intraocular pressure, which explains the high average mm Hg intraocular pressure values presented in Table I.

Xylocain Exadrin Concentrations of 1% (Group A) and 2% (Group B) were tested. Following retrobulbar injection a highly significant (***) reduction in μ and ΔV was demonstrated to average 26-31% of the value obtained before injection (Table I). A significant (*) decrease was also noted in the mm Hg intraocular pressure to average 87.5% (Group A) and 78.2% (Group B) of the value obtained before injection. A typical recording is presented in Figure 5.

No significant difference was found in μ , ΔV or mm Hg intraocular pressure between Group A and Group B as judged by the results obtained by application of the Student's *t* test which are summarized in Table III. This strongly indicates that a maximal corneal indentation pulse amplitude reducing effect is obtained with the 1% solution; no further reduction is to be expected by increasing the concentration to 2%. The fact that Xylocain Exadrin 1% contains 0.01 mg adrenalin per ml while Xylocain Exadrin 2% contains 0.0125 mg adrenalin per ml may probably explain the minor but not significant difference which exists between these two groups (Table I).

As seen in Table III there is a significant (**) difference in corneal indentation pulse amplitude reduction between Group A and C and between Group B and C as judged by the results obtained by application of the Student's *t* test. The decrease in amplitude is more pronounced in the two groups which received Xylocain Exadrin.

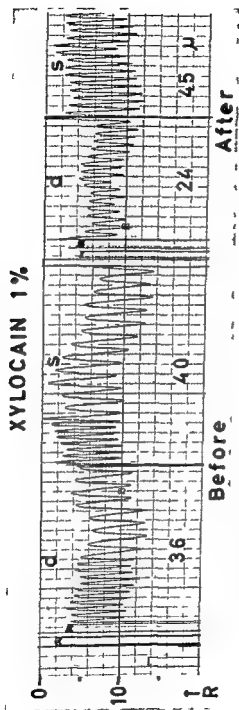


Fig. 3

Decrease in corneal indentation pulse amplitudes following right side retrobulbar injection of Xylocain 1%

Table IV
Visual acuity before and 8 minutes after retrobulbar injection of *Xylocain* 1%
(Group C $N=20$)

	5/20-5/15	5/20-5/30	c.t	1 p	nil
Before	13	5	2		
After	2	10	3	2	3

obtained before injection compared with 0.0189 after injection, with a t value of 1.502, as judged by the statistical method of paired comparison.

Discussion

A striking decrease of similar order of magnitude have been initiated in corneal indentation pulse amplitudes by retrobulbar injection of either *Ethadrin* or *Xylocain*. Evidence is offered suggesting that the two drugs act through different trigger mechanisms in their corneal indentation pulse amplitude reducing capacity, as a combined effect is obtained when the two drugs are injected simultaneously. In order to evaluate the mechanisms behind this effect, some possibilities may be excluded.

First, the injected volume of fluid may be ruled out as a possible cause to the decrease in amplitude, as there was no change in amplitudes in Group F which received saline. Second, a general effect of the drugs is not responsible for the decrease in amplitudes, because the corneal indentation pulse amplitudes as a rule were unchanged in the control mate eye as shown in Figures 1, 2, 3, 4. Third, it is known that a very low scleral rigidity may produce small corneal indentation pulse amplitudes (Syrdalen 1970). No significant change in scleral rigidity was, however, noted in our patients.

Fourth, it has previously been shown that the corneal indentation pulse amplitudes may change with the intraocular pressure levels (Horven 1970b). If the intraocular pressure (P_i) is higher than the systolic pressure in the ophthalmic artery, no blood will enter the eye and a zero amplitude will be recorded. As the intraocular pressure drops, the amplitudes will increase in size until a maximum is reached at a P_i value of 40-50 mm Hg. With a further drop in P_i , the amplitudes will decrease, this decrease is, however, rather limited in the normal range of intraocular pressure. As the present material contains eyes at various intraocular pressure levels, the slight decrease in intraocular pressure which in most cases was induced by the retrobulbar injection may have implied a minor change in corneal indentation pulse amplitudes. This change may be an increase or decrease in amplitudes dependent on the intraocular pressure levels before and after injection in the various eyes. No attempt has been

XYLOCAIN-EXADRIN 2%



Fig 5

Decrease in corneal indentation pulse amplitudes following left side retrobulbar injection of Xylocain Exadrin 2%

To summarize, the results demonstrate that a retrobulbar injection of Exadrin yields an average amplitude reduction to about 54% of the original values. A retrobulbar injection of Xylocain 1% or 2% yields a similar decrease in amplitude to about 50-60% of the value obtained before injection. However, if the Xylocain is injected after the Exadrin, or if the two drugs are injected simultaneously, a reduction in amplitudes to about 26-31% of the original values is obtained. It may therefore be concluded that Exadrin and Xylocain most probably act through different trigger mechanisms in their corneal indentation pulse amplitude decreasing capacity; the full effect of one of the drugs does not block the effect of the other drug.

Visual acuity Visual acuity was performed before and 8 minutes after injection of Xylocain 1% in Group C; a temporary decrease was found in 19 of the 20 patients and is listed in Table IV. All patients regained their original visual acuity when the effect of the anestheticum was subsided.

Scleral rigidity calculations demonstrated no significant change before and 10 minutes after retrobulbar injection of Xylocain Exadrin 1% in the 20 patients of Group A. An average scleral rigidity value of 0.0207 was

Table III

Comparison between Group A, B and C before and after retrobulbar injection
The table offers t values obtained by use of Student's t test

	μ		ΔV		mm Hg	
	Before	After	Before	After	Before	After
Group A/Group B	1.746	0.259	1.105	0.168	0.732	0.169
Group A/Group C	0.594	2.848**	0.821	2.389*	3.078**	2.507*
Group B/Group C	1.344	3.045**	1.116	2.786**	2.293*	2.025*

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(Group C $n=20$)

	5/5-5/15	5/20-5/50	cf	Ip	nil
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After	2	10	3	2	3

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made to evaluate the total effect on the amplitude sizes in our material which may be caused by the minor decrease in intraocular pressure following injection, as no proper method is available at present for such an evaluation. It is obvious, however, that the slight decrease in average intraocular pressure can explain only a minor and probably negligible part of the marked decrease in amplitudes following retrobulbar injection in our material.

It may be assumed that the corneal indentation pulse amplitudes primarily reflects the pulse synchronous change in ocular volume initiated by the excess of blood entering the eye in systole. Theoretically, if the blood flow was non pulsatile, i.e., if the same volume of blood entered the eye per time unit in diastole and systole, no pulsations would exist in the intraocular pressure and zero amplitudes would be recorded by dynamic tonometry, even if the total ocular blood flow was unchanged. It is quite possible that the decrease in corneal indentation pulse amplitudes observed following retrobulbar injection of xylocain may be caused by a change from pulsatile towards non-pulsatile blood flow, as xylocain possesses a vasodilatory effect (Dhuner & Lewis 1966, Goldman *et al* 1966).

On the other hand, if a decrease exists in the total ocular blood supply, this decrease would be reflected also in the pulsatile part with a corresponding decrease in corneal indentation pulse amplitudes. As known, Exadrin (adrenaline) stimulates both α (constrictor) and β (dilator) receptors. By the dose applied in the present study Exadrin most probably will induce vasoconstriction (de la Lande & Whelan 1959) with a corresponding reduction in ocular blood supply. If this view is valid the reduction to 54% in corneal indentation pulse amplitudes following retrobulbar injection of Exadrin is initiated by a corresponding decrease in ocular blood supply. Following intramuscular injection, Dhuner & Lewis (1966) found that the vasoconstrictor action of epinephrine did no more than offset the vasodilator action of Xylocain, the resultant blood flow was therefore not statistically significantly different from the saline control. It is stressed that the corneal indentation pulse amplitudes recorded by dynamic tonometry primarily reflects a pulse synchronous change of intraocular volume and offers no direct information upon ocular blood flow. The marked decrease of corneal indentation pulse amplitudes observed following retrobulbar injection of Xylocain Exadrin offers, therefore, no conclusive evidence upon the ocular blood flow through these eyes.

The reduction in intraocular pressure seen in our Group A, B and C is only confirming the observation known for long that retrobulbar anaesthesia is producing a certain degree of hypotonia. The cause of this

reduction has been explained from reduced inflow of aqueous humor (de Roeth & Carroll 1955) The reduced inflow of aqueous humor is partly produced by vasoconstriction caused by adrenaline (Duke Elder 1962) The hypotonia may also be caused by the anestheticum itself by blocking the parasympathetic activity of the third nerve and the ciliary ganglion (Gifford 1949) Atkinson (1961) explained lowered intraocular pressure as a result of decrease of blood within the choroid due to constriction of the arteries entering the globe

Carroll and de Roeth (1955) demonstrated a similar effect on visual acuity after retrobulbar anesthesia with procaine as observed in our Group C This effect is explained by absorption of the anestheticum into the optic nerve

Summary

A significant reduction in corneal indentation pulse amplitudes as recorded by dynamic tonometry is demonstrated following retrobulbar injection of either Xylocain, Exadrin or Xylocain Exadrin Evidence is offered suggesting that Exadrin and Xylocain act through different trigger mechanisms in their amplitude decreasing capacity the full effect of one of the drugs does not block the effect of the other drug

REFERENCES

- Atkinson W S The development of ophthalmic anesthesia *Amer J Ophthal* 51 1-14 1961
- Carroll F D and de Roeth A The effect of retrobulbar injections of procaine on the optic nerve *Trans Amer Acad Ophthal Otol* 59 356-365 1955
- de la Lande I S and Whelan R F The effect of antagonists on the response of the forearm vessels to adrenaline *J Physiol* 148 548-553 1959
- de Roeth A and Carroll F D Effect of retrobulbar procaine injection on aqueous humor dynamics *AMA Arch Ophthal* 53 399-403 1955
- Dhuner A G and Leurs D H Effect of local anaesthetics and vasoconstrictors upon regional blood flow *Acta anaesth Scandinav Suppl XXIII Proceedings I of the Second European Congress of Anaesthesiology* 1966 pp 347-352
- Duke Elder S *System of Ophthalmology* Vol VII The Foundations of Ophthalmology Henry Kimpton London 1962 p 572
- Dunn ngton J H Intraocular tension in cases of sarcoma of the chroid and ciliary body *AMA Arch Ophthal* 20 359-363 1938
- Gifford H A study of the effect of retrobulbar anesthesia on the ocular tension and the vitreous pressure *Amer J Ophthal* 32 1359-1368 1949
- Goldman I Ailey H C and Wright C Effects of local analgesic agents and vasoconstrictors on rabbits ears A preliminary Report *Acta anaesth Scandinav Suppl XXIII Proceedings I of the Second European Congress of Anaesthesiology* 1966 pp 353-365

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CAROTID CAVERNOUS FISTULAE

A Study of 18 Cases

By

P H Madsen

Pulsating exophthalmos is usually due to an abnormal communication between the internal carotid artery and the cavernous sinus. In most cases the condition develops after severe head injuries especially in the presence of fracture of the base of the skull, by which the internal carotid is injured in its course through the cavernous sinus. The relation between the artery and the surrounding sinus is so intimate that a lesion of the artery invariably results in entry of blood into the sinus, from which it is forced into the veins usually those entering the orbit. However, in from one quarter to one third of the patients the fistula occurs spontaneously (Hamby 1966, Stern, Brown and Alksne 1967, Sanders and Hoyt 1969). Traumatic fistulae are most frequently encountered in men whereas there is a female preponderance in the spontaneous group. It is likely that some of the spontaneous fistulae develop on rupture of an aneurysm in the intracavernous portion of the internal carotid artery. Jefferson (1938) even expressed the view that this was the causal mechanism in most carotid cavernous fistulae. Spontaneous fistulae occasionally develop during the latter part of pregnancy or during labour and arteriosclerosis seems to be a contributory cause in other cases.

Most commonly the disease is unilateral, but it may be bilateral if there is a wide communication between the cavernous sinuses on the right and left sides. Such inter cavernous communications are of normal occurrence but they are usually very narrow (Dandy 1937, Hamby 1966). In a few cases the fistula is followed by contralateral exophthalmos (David *et al* 1964, Graham 1966, Bynke 1969).

The manifestations are of fairly rapid onset occurring shortly after the trauma. Figure 1 shows a typical example of carotid cavernous fistula in a 22 year-old man. Very characteristic are the unilateral exophthalmos with pulsation of the eye and in step with the heart beats a pulse synchronous loud bruit in the same side of the head and above the orbit.

- Horven I* Dynamic tonometry I The dynamic tonometer, *Acta Ophthal (Kbh)* 46 1213-1221, 1968
- Horven, I* Dynamic tonometry and choroidal melanoma *A M A Arch Ophthal* 82 440-445, 1969
- Horven I* Dynamic tonometry II Methods of corneal indentation pulse registration *Acta Ophthal (Kbh)* 48 23-38 1970a
- Horven, I* Dynamic tonometry III The corneal indentation pulse in normal and glaucomatous eyes *Acta Ophthal (Kbh)* 48 39-58, 1970b
- Horven I and Syrdalen P* Corneal indentation pulse and general anesthesia *Acta Ophthal (Kbh)* 48 59-66, 1970
- McGowan, B L* Active temporal arteritis as a contraindication to elective surgery with general anesthesia, *Amer J Ophthal* 64 455-457, 1967
- Syrdalen, P* Corneal indentation pulse and retinal detachment *Acta Ophthal (Kbh)* in press, 1970

important to ensure that there is blood supply to both halves of the brain. Conditions which require differentiation are orbital encephalocele, lacrimal orbital tumour, tumour of the optic nerve and meningioma of the optic nerves, which produce symptoms which are reminiscent of those of carotid-cavernous fistula (Walsh 1957, Higazi and El Banhawy 1964, Ambly 1966). I have observed distinctly pulsating exophthalmos in two patients in whom the orbital roof has been removed after traumatic injury, but angiography did not reveal a fistula in these patients.



Fig 2

Right common carotid angiogram showing carotid-cavernous fistula draining to orbital veins in a 65 year-old man (Case 6) (Subtraction angiogram)

The disease is treated by producing thrombosis in the arteriovenous communication.

1 Spontaneous thrombosis may be seen in rare cases (Knudtzon 1950). Dandy (1937) reported that spontaneous healing occurred in 10%, but this figure is too high. In his analysis, he included patients who had been

The marked hyperaemia of the cavernous sinus and the orbital veins is transmitted to the vessels on the forehead and in the conjunctiva, resulting in large, tortuous, dilated veins and lid oedema



Fig 1

Left sided carotid cavernous fistula in a 22 year old man (Case 8)

In relation to the pulsating exophthalmos, disturbances of the ocular movements often occur. Paresis involves the abducent nerve more frequently than the oculomotor and trochlear nerves. However, in many cases, the limitation of ocular movements is of a mechanical nature, due to orbital oedema. Vision is frequently impaired, and atrophy of the optic nerve may occur. Ophthalmoscopic examination reveals marked venous congestion and, sometimes, mild papilloedema and extravasation of blood. Secondary glaucoma may also be observed in rare cases (Henderson and Schneider 1959, Sanders and Hoyt 1969).

Even though the fistula may produce greatly discomforting symptoms, it is an immediate advantage for the patient that the arterial blood, instead of entering the cranial cavity, passes direct into the veins. However, this involves the risk of vascular insufficiency in the region of the brain which is supplied by the upper portion of the internal carotid, with ensuing cerebral manifestations. Another complication is venous congestion in the nasal cavity, which may lead to fatal epistaxis.

The diagnosis is made on the basis of the typical clinical picture and carotid angiography (Fig 2). By angiography on the contralateral side it

is important to ensure that there is blood supply to both halves of the brain. Conditions which require differentiation are orbital encephalocele, vascular orbital tumour, tumour of the optic nerve and meningioma of the olfactory nerves, which produce symptoms which are reminiscent of those of carotid cavernous fistula (Walsh 1957, Higazi and El Banhawy 1964, Hamby 1966). I have observed distinctly pulsating exophthalmos in two patients in whom the orbital roof has been removed after traumatic injury, but angiography did not reveal a fistula in these patients.



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subjected to operation, but in whom healing occurred later than three weeks postoperatively

2 *Prolonged compression of the internal carotid in the neck* was previously a commonly used method (Hamby 1966, Isfort 1967) It was recommended by Dandy in cases in which it was desired to avoid even a small operation

3 *Ligation of the common and, possibly, the external carotid*

4 *Ligation of the internal carotid in the neck*

Until a few years ago, procedures 3 and 4 were the most commonly used therapeutic measures

5 *Ligation of the internal carotid in the neck and intracranially above the fistula (trapping operation)* In this operation, an attempt is made to place the ligature caudalward to the ophthalmic artery, but sometimes it is also necessary to ligate the latter

6 *Ligation of the internal carotid in the neck and, perhaps, also intracranially, supplemented by muscle embolisation of the fistula* (Brooks 1931, Hamby 1964, 1966) A silver clipped muscle strip is introduced into the internal carotid and forced up to the fistula, which is then closed

7 *Embolisation by other agents, such as gelfoam or radio opaque measured beads*

8 *Direct intervention on the cavernous sinus or excision of orbital veins*

Clinical Material

The series studied consisted of 18 patients with carotid cavernous fistula, 12 from Aarhus Kommunehospital and six from Odense Amtssygehus In 17 cases, the fistula was confirmed by carotid angiography, while this method of examination was not used in the last patient, a 72 year-old woman, who was not subjected to operation

Clinical data concerning the 18 patients are listed in Table 1 (before treatment) and Table 2 (after treatment) There were 13 men and five women In two of the women, the fistula occurred spontaneously without any demonstrable preceding trauma, while, in the remaining cases, the carotid cavernous fistulae were referable to severe head injuries, in 10 of the patients, fracture of the base of the skull was present

Carotid cavernous fistulae may be encountered in all age groups The fistula was situated on the right side in 11 cases and on the left side in six, while bilateral fistulae were seen in one Fourteen patients had unilateral ocular symptoms on the ipsilateral side, while three had a unilateral fistula with bilateral ocular symptoms (Cases 2, 10 and 12)

Spontaneous fistula occurred in two women aged 63 and 49 years In the first of these patients, carotid angiography revealed a hazelnut sized saccular aneurysm on the internal carotid at the cavernous sinus (Figs 3 and 4) Marked exophthalmos, lid oedema, abolition of ocular move-

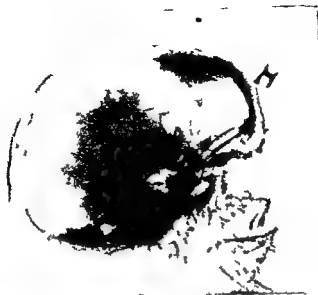


Fig 3

Right common carotid angiogram with saccular aneurysm (arrow) in the cavernous sinus and drainage to a very dilated orbital vein in a 63 year-old woman with spontaneous carotid cavernous fistula (Case 1)

ments and corneal anaesthesia were present, and there was absolute glaucoma of the eye (Fig 5). After ligation of the common carotid artery the exophthalmos and the orbital and lid oedema resolved but ophthalmoplegia and corneal anaesthesia persisted and the eye remained blind (Fig 6). In the second patient no carotid aneurysms were demonstrated.

In the remaining 16 patients the fistulae were of traumatic origin. The nature of the traumata sustained appears from Table 1. The symptoms of the arteriovenous fistula developed from a few days to weeks after the accident. Table 1 also shows the time when exophthalmos was first observed. In most cases paresis of the ocular muscles and a bruit synchronous with the pulse developed within a few days while exophthalmos and lid oedema occurred later.

One of the patients, a 26 year old man (Case 15) suffered from mild arterial hypertension and the five oldest patients in the series (Cases 6, 12, 13, 17 and 18) revealed radiographic signs of aortic and carotid arteriosclerosis.

Lid oedema and dilated tortuous vessels in the conjunctiva and orbital region were observed in all patients (Fig 7). With just one exception (Case 1) a pulse synchronous bruit — observed by the patients and recognised by auscultation — was present in all cases causing great discomfort.



Fig 4

Anteroposterior view of the same patient (Arrow indicates the aneurysm)

to the patients *Exophthalmos* was also present in all except one (Case 14) This patient had dilated, pulsating vessels in the eyelid and conjunctiva and oedema of the orbital region In most of the patients, the exophthalmos was fairly distinct, measuring 5–10 mm as compared with the other eye Two patients had exophthalmos, but no pulsation (Cases 1 and 15) The pulsation was occasionally very slight For example, in Case 2 it could be recognised only under the slit lamp The remaining patients had distinct pulsation of the eyeball and the vessels in the medial canthus

The ocular manifestations were unilateral in 14 patients One patient had bilateral fistulae and bilateral exophthalmos In three cases, the fistula was unilateral, but was accompanied by bilateral ocular signs Strikingly enough, in these patients (Cases 2, 10 and 12) the pulsating exophthalmos and the palpebral and conjunctival oedema were most pronounced on the contralateral side In Case 10, even post traumatic



Fig 5

Right sided spontaneous carotid cavernous fistula in a 63 year-old woman (Case 1)

enophthalmos developed on the affected side to be followed later by proptosis of the eye

Visual acuity in the patients before the treatment is listed in Table 1. It is seen that it ranged from 0.5 to 1.0 in 12 eyes in 11 patients, and one had a vision of 0.25. In three patients it was impossible to determine the visual acuity. Three patients had no light perception in the five affected eyes, one of these had absolute glaucoma and another was blind because of a direct trauma to the eye. All patients with unilateral symptoms revealed a visual acuity ranging from 0.67 to 1.0 in the unaffected eye.



Fig 6

The same patient five months after ligation of the common carotid artery (Case 1)



Fig 4

Anteroposterior view of the same patient (Arrow indicates the aneurysm)

to the patients *Exophthalmos* was also present in all except one (Case 14). This patient had dilated, pulsating vessels in the eyelid and conjunctiva and oedema of the orbital region. In most of the patients, the exophthalmos was fairly distinct, measuring 5–10 mm as compared with the other eye. Two patients had exophthalmos, but no pulsation (Cases 1 and 15). The pulsation was occasionally very slight. For example, in Case 2 it could be recognised only under the slit lamp. The remaining patients had distinct pulsation of the eyeball and the vessels in the medial canthus.

The ocular manifestations were unilateral in 14 patients. One patient had bilateral fistulae and bilateral exophthalmos. In three cases, the fistula was unilateral, but was accompanied by bilateral ocular signs. Strikingly enough, in these patients (Cases 2, 10 and 12) the pulsating exophthalmos and the palpebral and conjunctival oedema were most pronounced on the contralateral side. In Case 10, even post traumatic

[illegible]

Table 1
Data concerning the 18 patients with carotid cavernous fistula

<i>Case</i>	<i>Sex</i>	<i>Age, Side</i>	<i>Type</i>	<i>Trauma</i>	<i>Exophthalmos after trauma No. of days</i>	<i>Exophthalmos</i>	<i>Chemosis dilated tears</i>	<i>Visual Brust acuity</i>	<i>Mobility of the eye</i>	<i>Ophthalmoscopy</i>
1	F	63	R	Spontaneous		+	(no pulsation)	+	No movements	Extensive haemorrhage
2	F	49	R	Spontaneous		RE +	(+) + 10	+	VI paresis	Slight venous stasis
3	M	17	L	Traumatic	Fall 3 metres 14	LE +	+	+	VI paresis	Normal
4	F	16	R	Traumatic	On bicycle hit by car 12	+	+	+	VI paresis	Normal
5	M	29	L	Traumatic	Motor cycle accident 6	+	+	+	III + IV paresis	Normal
6	M	65	R	Traumatic	Moped accident 30	+	+	+	Slight diplopia	Venous stasis Venous stasis blurred disc
7	M	16	L	Traumatic	Horner's synd accident 60	+	+	+	VI paresis	Venous stasis blurred disc
8	M	54	R	Traumatic	Moped accident 7	+	+	+	Impaired movements	Venous stasis slight oedema
9	M	22	L	Traumatic	Bicycle accident 30	+	+	+	Impaired movements	Slight venous stasis
					Car accident 1	+	+	+	VI pa	Slightly blu red

Exophthalmos had been present in 14 patients. Within a week after operation it disappeared completely in 10 (13 eyes) and abated to some extent in two. These two patients did not return for follow up examination and did not answer inquiries by letter. In two patients, the exophthalmos subsided, but recurred later, and in spite of several subsequent operations pulsating exophthalmos persisted, although it was less severe than before the surgical intervention (cases 3 and 15).

Oedema of the eyelid, conjunctiva and orbital region and dilated veins in the eyelid and conjunctiva disappeared completely in eleven and abated in four after operation.

Pulse synchronous bruit disappeared postoperatively in all patients except one (Case 8), in whom it was, however, considerably less severe one week after ligation of the internal carotid artery.

Vision was normal in most of the patients before operation (0.5-1.0 in nine patients - 10 eyes). No postoperative improvement was obtained in two patients (Cases 1 and 10, no light perception). Three weeks after operation improvement from no light perception to counting of fingers at 2 metres occurred in both eyes in Case 12. In Case 5, the vision improved from 0.25 to 1.0.

Gradual deterioration of vision was observed post-operatively in two patients after ligation of the common carotid (Cases 6 and 15). About two years later both revealed optic atrophy and 3-4 years later vision was determined as no light perception in one and counting of fingers at 0.5 metre in the other.

Ocular movements improved postoperatively in most of the patients. However it should be noted that paresis of the abducent nerve persisted for several months in some cases (Table 2).

The retinal changes resolved or abated postoperatively in most eyes. However it is worthy of note that in Case 2 transient venous stasis and retinal oedema developed after ligation of the internal carotid, and that considerable aggravation with increased venous stasis and papilloedema accompanied by numerous haemorrhages and tiny cotton wool exudates was observed after ligation of the common carotid in two patients (Cases 6 and 15). Ophthalmodynamometry revealed a reduced pressure in the ophthalmic artery in the older of the two patients. Two years later optic atrophy accompanied by severe visual impairment had developed in both cases.

Pre operatively corneal sensibility was lost in one patient and impaired in two. In Case 1 anaesthesia of the cornea and of the first branch of the trigeminal nerve persisted after operation. In the other two patients the corneal sensibility was normal at the follow up examination. Postoperative corneal hypaesthesia developed in two patients (Cases 6 and 15).



Fig 7

Conjunctival changes in a 26 year old man with right sided fistula (Case 15)

Most of the patients had noticed *diplopia*, and all had limitations of ocular movements. Paresis of the abducent nerve was present in seven, of the abducent and oculomotor nerves in two, and complete loss of ocular movements was observed in eight.

Corneal sensibility was lost in one patient and impaired in two.

Ophthalmoscopy revealed a normal fundus in seven eyes, while venous stasis and/or slight papilloedema were present in 11. One patient with spontaneous carotid cavernous fistula (Case 1) had extensive retinal haemorrhages, which resolved postoperatively, but then a glaucomatous cupped disc was observed. Case 10 had a large vitreous haemorrhage after a direct trauma to the eye sustained a few months before, when a badminton ball had hit his eye.

One patient had absolute *glaucoma*. In four patients, the intra ocular pressure had been measured before operation, and it was increased in all four (6-7 mm Hg higher than in the opposite eye). In two of these patients, the tension was measured postoperatively, it had then decreased to normal values in both cases. Rubeosis iridis was observed in one patient (Case 6).

Surgical Treatment

Operation was performed in 15 patients, and an account of the effect on the individual signs is given below.

Table 2 shows the surgical procedures applied and their effect as assessed at the last follow up examination.

11	Internal carotid ligation	+	2 months	?	VI par s	No mal
12	Muscle embolisation and internal carotid ligation	RE + LI +	3 weeks	1 ct 2 m 1 ct 2 m III + VI parcaus	Normal Normal	Normal
13	Spontaneous thrombosis of cavernous sinus	+	3½ years	0.5	Normal	During cavernous thrombosis severe retinopathy after 3½ years senile macular degeneration
14	Internal carotid ligation later trapping later external and common carotid ligation	+	3 years	1.0	Normal	Normal
15	Common carotid ligation later internal carotid ligation followed by trapping and stepwise ligation of arteries (external carotid superior thyroid dorsal nasal supraorbital and superior palpebral arteries)	(+)(exoph. bulb)	3 years	1 ct 0.5 m	Normal	Retinopathy had aggravated later atrophy of the optic disc
16	Muscle embolisation by the method of Hamby (1966)	+	1½ years 4½ months	0.67 1.0	VI parcaus VI parcaus	Normal No change
17	No treatment		Dead	?		
18	No treatment — the patient died after a few days					

Table 2
Data after treatment at the last control

Treatment	Effect on pulsation exoph, brunt	Follow up	Visual acuity	Motility	Fundus
1 Common carotid ligation	+	8 years	No LP	Severely impaired movements	Glaucomatous cupped disc
2 Internal carotid ligation later trapping	RE +		10	Slight VI paresis	Normal
3 Common carotid ligation later internal carotid ligation	LE +	5 months	10	Normal	Normal
4 Internal carotid ligation	+	3½ years	10	Normal	Normal
	+	4 years	10	Normal	Venous stasis and oedema — normal
5 Common carotid ligation later ligation of internal carotid later trapping and orbitotomy (+)(exoph)		10 years	10	Normal	Normal
6 Common carotid ligation	+	4 years	No LP	Total VI paresis	Retinopathy had aggravated, later atrophy of the optic disc
7 Internal carotid ligation	+	3½ years	10	Normal	Normal
8 Internal carotid ligation	(+)	1 week	0.67	Diplopia	No change
9 Internal carotid ligation	(+)	1 week	10	Normal	No change
10 Common carotid ligation later internal carotid ligation	RE +	Dead after 8 days	No LP	?	Normal
	LE +	Dead after 8 days	No LI	?	Vitreous haemorrhage

Discussion

It is noteworthy that in two cases of this series, ligation of the common carotid artery was followed by distinct aggravation of the venous stasis and haemorrhages and cotton wool exudates in the fundus. These changes were also present in the patients at a follow up 4-5 months later. In the other surgical patients, the venous stasis and papilloedema regressed shortly after the intervention.

Patients with carotid cavernous fistula are marked by greatly blood-filled veins, and it should therefore be expected that ligation of the afferent artery would result in cessation of the venous stasis. This, in fact, also occurs in most cases, but some examples are on record in which ligation of the common or internal carotid has led to aggravation of the retinopathy (Knapp 1901 Ruata 1916, Augstein 1916 Jaensch 1924 Swan and Raaf 1951, Schenk 1955, Holst (Case 2) 1960 Renpenning and Wacasar 1963, Mooney 1965 Sanders and Hoyt 1969).

The development of this retinopathy may have several causes. In the German literature special emphasis is placed on the similarity to Purtscher's retinopathy which is referable to a suddenly increased venous pressure after head or chest injuries. In his two patients Schenk (1955) explained the retinopathy as a consequence of a recurrence of sudden onset. Other authors e.g. Swan and Raaf (1951) expressed the view that venous stasis and retinopathy were consequences of arterial hypotension and Sanders and Hoyt (1969) also emphasised that hypoxia is an essential factor in the development of the ocular manifestations in carotid cavernous fistula and that surgery may very well increase this hypoxia. Stern, Brown and Allsne (1967) pointed out that cerebral hypoxia mainly occurred after ligation of the carotid in the neck alone. If it is this arterial hypotension which is the cause of the aggravation of the venous stasis and retinopathy it must be of the same nature as that seen on occlusion of the carotid artery (Kearns and Hollenhorst 1963) and the ophthalmic artery (Madsen 1966).

The two patients in the present series with pronounced aggravation in the ophthalmoscopic appearance had in fact several signs of hypoxic ocular disease.

One of the patients had, although he was only 26 years old a slightly increased blood pressure and the other aged 65 had arteriosclerosis. In both cases diminished corneal sensibility was observed after operation and gradual impairment of vision occurred. The older of the two patients lost light perception and in the younger vision was reduced to counting of fingers at 0.5 metre after three years. Ophthalmoscopy performed 4-5 months postoperatively revealed the persistence of mild papilloedema, venous stasis, haemorrhages and exudates. The retinopathy with several

Ophthalmodynamometry was performed in five patients postoperatively. The pressure in the ophthalmic artery was reduced to from one third to one half of normal on the side subjected to operation, but no definite correlation between the pressure in the ophthalmic artery and visual acuity was observed. The lowest diastolic pressure (10 mm Hg) was measured in Case 5, who had preserved a vision of 1/0.

The *treatment* applied in the 15 cases appears from Table 2. Ligation of the internal or common carotid was performed in seven cases, which resulted in subsidence or complete disappearance of exophthalmos. In another six patients the primary ligation of the internal or common carotid had to be supplemented by further ligations. A good result was obtained by primary muscle embolisation of the fistula in two patients (Cases 12 and 16). In Case 12, a silver-clipped muscle strip was introduced through the internal carotid into the fistula by means of an embolectomy catheter (Prof Malmros). In Case 16, ligation of the internal carotid was performed intracranially, with introduction of a muscle embolus into the internal carotid and ligation of the common, internal and external carotids in the neck (Dr Husby). Postoperative radiography showed that in both cases the muscle embolus was at a level with the fistula. Case 16 will be published elsewhere (Olsen 1969).

In one patient (Case 5), epilepsy developed after several operations on the vessels in the neck and intracranially. The operations did not give rise to severe hypoxic cerebral lesions in any of the other patients.

No Treatment

No treatment was given in three patients. One died after a few days in hospital (Case 18). In another, the condition was unchanged after the lapse of 4½ months (Case 17). The third patient was a 72-year old woman in whom left sided carotid cavernous fistula developed, after head injuries with fracture of the skull (Case 13). Three weeks later, thrombosis of the cavernous sinus led to fever and increased protrusion of the left eyeball. In connection with the increased protrusion the pulse synchronous bruit ceased. There was transient aggravation of the retinopathy with disc swelling, markedly dilated veins and flame shaped haemorrhages. The symptoms of the thrombosis of the cavernous sinus resolved within a month, and so did the signs of carotid cavernous fistula. In this patient with a typical carotid cavernous fistula, spontaneous thrombosis of the cavernous sinus resulted in closure of the fistula.

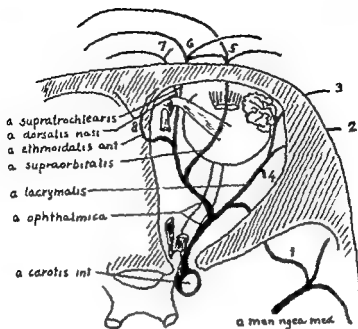


Fig 8

Anastomoses between the ophthalmic artery and the external carotid artery

- 1 Recurrent meningeal branch of the lacrimal artery to the middle meningeal artery
- 2 Zygomatico-temporal branch of the lacrimal artery to the anterior deep temporal artery which arises from the internal maxillary artery
- 3 Zygomatico-facial branch of the lacrimal artery to the transverse facial artery from the superficial temporal artery
- 4 Branch from the lacrimal artery to the infra-orbital artery from the internal meningeal artery
- 5 Supra-orbital artery anastomoses with the supra-orbital artery of the other side the supratrochlear and the superficial temporal arteries.
- 6 Supratrochlear artery anastomoses with the supra-orbital and the superficial temporal arteries as well as the supra trochlear artery of the other side
- 7 Dorsal nasal artery anastomoses with the facial artery and the artery of the other side
- 8 Anterior ethmoidal artery gives off the anterior meningeal artery which anastomoses with the middle meningeal artery

Figure 8 is a diagrammatic representation of the ophthalmic artery with the anastomoses to the internal and external carotid arteries. Of great importance is the communication between the middle meningeal and the lacrimal arteries. The ophthalmic artery is sometimes supplied mainly or exclusively by this route (Hayreh and Dass 1962, Hayreh 1962, Walsh 1957, Jarvesson 1964). Most of the other communications are narrow but may if need be take over the blood supply to the ophthalmic artery and the eye. After spontaneous thrombosis of the internal carotid,

small haemorrhages, red points and a few cotton wool exudates was more reminiscent of that described after occlusive vascular disorders than of the more violent exudative picture which is often observed in Purtscher's retinopathy (Madsen 1965, 1966). Optic atrophy was present in both patients 3-4 years later.

In these two patients, who had pre-existing arterial disease, ligation of the common carotid artery had resulted in severely reduced blood supply to the ophthalmic artery.

In some cases, the aggravated retinopathy may, in addition to arterial hypotension, be referable to thrombosis of the cavernous sinus and the orbital veins. In Case 13, spontaneous closure of the fistula occurred after a cavernous sinus thrombosis, which was followed by retinopathy of an appearance as that seen in central-vein thrombosis.

Until recently, treatment of carotid cavernous fistula consisted mainly in ligation of the common or internal carotid artery in the neck. This procedure was also used in 13 patients in the series considered here. This primary ligation was satisfactory in seven cases, but in the other six it had to be supplemented by other measures. Ligation of the common carotid seems particularly to be insufficient as the only procedure. It must be assumed that the unsuccessful surgical results were due to the presence of well developed anastomoses to the cranial portion of the internal carotid. The most important communication is the circle of Willis, which is supplied from the contralateral internal carotid and from the basilar artery. Other anastomoses between the internal carotid and the basilar artery may occasionally be present, viz. primitive vessels (trigeminal and hypoglossal arteries) which have not been obliterated after the development of the posterior communicating artery. In the cavernous sinus, the internal carotid gives off several small vessels which anastomose with the contralateral internal carotid and with external vessels, such as the middle meningeal artery. The lack of success of repeated operations in Case 5 was possibly due to the presence of some of these vessels.

Furthermore, a considerable part of the blood supply to the upper portion of the internal carotid may come from the external carotid through the ophthalmic artery. This is one of the reasons why, in intra-cranial ligation of the internal carotid (trapping operation), an attempt is made to place the ligature caudalward to the origin of the ophthalmic artery, or why it may also be necessary to ligate this vessel. In some patients, the ophthalmic artery can be ligated at the origin without causing blindness of the eye. This can be done only because of the presence of wide anastomoses to the external carotid. The ophthalmic artery is an "arterial bridge" with well developed communications to both the internal and external carotids (Rushede 1957, Krayenbuhl and Yasargil 1965).

aggravation of the retinopathy and subsequent optic atrophy, probably due to hypoxia, were observed in two cases

Vision was unchanged in 11 patients after operation, improvement occurred in two and deterioration in two

Spontaneous thrombosis of the cavernous sinus with closure of the fistula occurred in one of the patients who were not subjected to operation. A saccular carotid aneurysm was observed in one of the patients with fistula of spontaneous origin

Owing to the numerous possibilities of anastomoses, ligation of vessels had to be repeated in five cases in order to obtain an acceptable result. Accordingly, it is desirable to perform a direct operation on the fistula at once

REFERENCES

- Augstein H. *Klin Mbl Augenheilk* 1916 56 484-492
- Brooks B. Discussion. Noland L and Taylor A S. *Trans South Surg A* 1931 43 116-177
- Bynke H. *Danish Ophthalm Soc and Sydsvenska Oftalmologklubben Lund, febr* 1963
- Dandy W E. *Zentralbl f Neurochirurgie* 1937 2 77-113 165-206
- David M, Metzger J, Michel F and Pradat P. *Neurochirurgia* 1964 7 86-95
- Echols W H and Jackson J D. *J Neurosurg* 1959 16 619-624
- Graham M I. *Brit J Ophth* 1966 50 599-602
- Hamby W B. *J Neurosurg* 1964 21 859-866
- Hamby W B. *Carotid Cavernous Fistula*. Charles C Thomas Springfield 1966
- Hayreh S S and Dass R. *Brit J Ophth* 1962 46 65-98 165-185
- Hayreh S S. *Brit J Ophth* 1962 46 212-247
- Henderson J W and Schneider R C. *Am J Ophth* 1959 48 585-597
- Hoga J and El Danhouy A. *J Neurosurg* 1964 21 561-566
- Holst H. *Acta Ophth* 1960 38 686-697
- Jacobsen H H and Skinhøj E. *Danish Med Bull* 1957 4 240-248
- Jansch P A. *Klin Mbl Augenheilk*, 1924 73 251-252
- Jamieson A G. *Aust New Zeal J Surg* 1964 34 1-10 quoted by Kearns T P
- Arch Ophth* (Chicago) 1965 74 707-738
- Jefferson G. *Brit J Surg* 1938 26 267-302
- Kearns T P and Hollenhorst R W. *Proc Staff Meetings of the Mayo Clinic* 1963 38 304-317
- Knepp P Z. *Augenheilk* 1901 6 466-473
- Knudsen A. *Acta Ophth* 1950 28 363-369
- Krimmhubl H and Yasargil M G. *Die zerebrale Angiographie. Lehrbuch für Klinik und Praxis*. Georg Thieme Stuttgart 2nd. Ed 1965
- Madsen P H. *Acta Ophth* 1965 43 776-786
- Madsen P H. *Acta Ophth* 1966 44 940-947
- Mooney S and Mooney M. *Arch Ophth* (Chicago) 1965 73 746
- Olsen J. *Ugeskrift f Læger* 1969 131 1984-1986
- Rosenburg H J and Macasay L E. *Arch Ophth* (Chicago) 1963 69 186-190

such anastomoses between the external carotid and the ophthalmic artery are often observed. In such cases, angiography of the common carotid reveals an occlusion of the internal carotid artery, but filling of the external branches, and through the ophthalmic artery, also of the carotid siphon and the intracerebral vessels (Rushede 1957, Rushede, Ottosen and Sondergaard 1960, Jacobsen and Skinhøj 1957). However, Rushede (1957) reported that the communications between the external carotid and the ophthalmic artery were established through the internal maxillary artery, not through the facial or middle meningeal arteries.

In view of all these possibilities of the formation of anastomoses, it is not surprising that operation on the cervical vessels alone may be followed by recurrence. At subsequent operations, such anastomoses may have formed, and it may be necessary to ligate vessels, one by one, in successive operations without achieving closure of the fistula, as was seen in two patients of the present series (Cases 6 and 15). Better procedures are (1) the trapping operation with simultaneous ligation of the internal carotid both in the neck and intracranially, preferably in such a way that the ophthalmic artery is spared, or (2) muscle embolisation in combination with ligation of the internal carotid artery. Furthermore, as emphasised by Sanders and Hoyt (1969), a pre-operatively increased intra ocular pressure should presumably be reduced in relation to the ligation of the carotid vessels. Otherwise, a disproportion between the high intra ocular pressure and the low pressure in the arteries after the ligation may easily arise, and this may lead to serious consequences, especially in the presence of pre-existing arterial affection.

Summary

A study on a series of 18 patients with carotid cavernous fistula is presented. Of the cases, 16 were of traumatic origin, while two were of spontaneous onset. One patient had bilateral fistulae. In the remaining 17 patients, the fistula was unilateral, but three of these patients had bilateral manifestations.

Thirteen patients were treated with ligation of the carotid vessels, and two with ligation and muscle embolisation. Lasting effect on the pulsating exophthalmos was obtained in 11 patients, in two the effect was incomplete in spite of repeated operations. Two patients did not return for follow up examination.

Bruit disappeared in all patients but one. There was also improvement of the eye movements in most patients.

The retinal changes disappeared in most of the cases. Postoperative

ophthalmica sin to be filled with a cohesive somewhat whitish thrombus formation attached to the wall and very brittle. The frontal sinuses were clear on both sides. There was a considerable injection of the middle cranial cavity particularly above the cavernous sinus and down the lateral wall to the sphenoidal bone. The intercavernous sinuses were also full to the brim of thromboses.

Conclusion from section A conclusive cavernous sinus thrombosis on a septic foundation with localized basal meningitis. The thrombosis began on the left side and spread to the right through the intercavernous sinuses.

Six years ago a similar case was admitted to the Department a 34 year-old man with initial shock from a nasal furuncle who recovered after intensive antithrombotic and antibiotic treatment.

I have personally seen a total of 4 such cases all men. In 1936 400 cases of cavernous sinus thrombosis were collected from all over the world all mortal. In 1937 the first case was successfully treated with sulpho. Anticoagulation treatment was first introduced in 1941 by Lyons(1). The first case to be completely cured with penicillin was described by Goodhill(2) in 1944.

In 1948 the literature of this complaint was supplemented by 60 cases of documented cavernous sinus thrombosis. 53 patients of 88% recovered although only 23% of these without serious complications or residual abnormalities. These cases were presented by Shaw(3) who states that this degree of comparative restitution is on the whole unduly high.

The primary foci of infection were Furuncles on cheeks forehead nose lips and eyelids. Also sinusitis with nasal infection, otitis dental infection facial injuries and in a small number of cases more remote infection.

The sequelae were Amaurosis ophthalmoplegia ptosis and atrophy.

The solution is diagnosis at the earliest possible moment and only a combination of antibiotic and antithrombotic treatment started at an early stage can save the patient. Diagnosis cannot always be left to more refined and sophisticated special examinations but must be made at the bedside as early as possible by an experienced specialist.

1 Lyons C Ann Surg 113 113 1941

2 Goodhill V A.M.A 125 28 1944

3 Shaw R E Cavern. sin tromboflebitis Arch Otolaryng 51 917-924 1948

- Rushede, J Acta Psychiat Neurol Scand 1957 32, suppl 118
 Rushede, J Ottosen, P and Søndergaard, T Danish Med Bull 1960 7, 185-192
 Ruata, V Klin Mbl Augenheilk 1916 56, 608-609
 Sanders, M D and Hoyt, W F Brit J Ophth 1969 53 82-97
 Schenk, H Klin Mbl Augenheilk 1955 127, 669-676
 Siebeck, R and Wollensak, J Klin Mbl Augenheilk 1960 136, 852-855
 Stern, W E, Broun, W J and Allsne, J F J Neurosurg 1967 27, 298-308
 Swan, A C and Raaf, J Trans Am Ophth Soc 1951 59, 435-444
 Walsh, F B Clinical Neuro Ophthalmology 2nd Ed 1957 Williams and Wilkins, Baltimore
 Wolff, E Anatomy of the Eye and Orbit 5th Ed Revised by R L Last 1961 Lewis & Co London

Discussion

T Waalen (Gjovik)

CAVERNOUS SINUS THROMBOSIS

When one has followed for decades the positively explosive developments in the special fields of medicine, not least in ophthalmology, one cannot help being struck by the wealth of material put forward in the course of these few days concerning the orbit and neuro ophthalmology

We have heard that the orbit has no lymph tracts that its venous channels are not supplied with valves, and that they drain into the cavernous sinus via the vena ophtal mica sup and posterior If there is good communication between the vena angularis and the vena ophtalmica infectious processes from the nose and facial region will be able to spread easily and quickly to the orbit and to the cavernous sinus

What will this mean for clinical practice and for the future? It seems likely that the increasing number of head injuries, with open lesions in the skin and mucous membranes, will lead to such serious processes becoming more common A case admitted some months ago to the Department where I work shows how important it is that the ophthalmologist enters the picture as soon as possible

Early diagnosis is a decisive factor in prognosis and it may well be the eye specialist who saves the day

A 24 year old man became suddenly ill with pyrexia, slimy secretion from the left nostril, red and swollen nose for 8-10 days On admission to the Department he had a small lesion in the left vestibule of the nose He had been treated for 3-4 days by a general practitioner with doses of penicillin On being admitted to the Department for Sinusitis he had a high temperature a red and swollen left nostril and venous stasis in the left conjunctiva In the course of the evening and night venous stasis also developed in the conjunctiva of the right eye In the early morning of October 13 1969 he became comatose and had a rectal temperature of 41.7 The eye grounds showed markedly congested veins like thick sausages no appreciable prominence or oedema of the optic discs An X ray showed clear sinuses The clinical diagnosis was cavernous sinus thrombosis and apparatus maxima was set in with 10 ml antibiotics every 4th hour Heparin 3 ml intravenous + Streptomycin $\frac{1}{2}$ g \times 2 + Chloramphenicol succinate 1 g \times 4 Antiphlogistic treatment with Largactil was given the sickroom was cooled and a freeze mattress was employed

No reversal of the condition occurred and death took place at about 10 a.m preceded by jerking of the arms and legs Section showed the cavernous sinus and vena

patients and one as an out patient in various clinics of the University Hospital Lund, because of extraocular and ocular symptoms. One single patient lacked extraocular symptoms and was referred to us from another ophthalmologist because of blurred and elevated discs. In all the cases ocular examinations were made by us one or several times. Papilloedema existed in 16 patients. In 9 the oedema was due to brain tumour verified by surgery, in 2 to cerebral trauma, in one to encephalitis and in one to arterial hypertension. Three patients, in whom the cause of the papilloedema remained obscure, deserve special reports.

Case 8 a woman of 48 had been examined in this hospital in 1956 because of headache, arterial hypertension and papilloedema of 3-4 D. On that occasion a brain tumour was suspected but could not be confirmed. The papilloedema decreased spontaneously over some months but did not disappear. In November 1968 she was again hospitalized because of spontaneous liquorrhea. A general neurological examination was negative. The blood pressure was 220/120 mm Hg. The visual function was normal. The optic discs were blurred, elevated 1 D and a little pale. The retinal arteries were narrow and there were marked arterio-venous crossing defects but no haemorrhages. Encephalography did not reveal any brain tumour. She was recommended further investigation but did not accept, partly since the liquorrhea had disappeared after repeated lumbar punctures.

Case 19 a man of 58 was referred to this hospital because of headache, arterial hypertension and papilloedema. A general neurological examination was negative. The blood pressure was 180/110 mm Hg. The visual function was normal. The optic discs were hyperaemic, blurred and elevated 3 D (R.E.) and 2 D (L.E.). The retinal arteries were narrow and the veins dilated. There were crossing defects and juxtapapillary hard exudates but no haemorrhages. The ventricular fluid pressure was normal. Angiographic and encephalographic examinations did not reveal any brain tumour. The patient was discharged and antihypertensive medicine prescribed. About one month later a slight regression of the papilloedema was noted.

Case 22 a woman of 51 had been suffering from dizziness for many years. Repeated examinations in another hospital had been negative until 1956 when the discs were found to be blurred. A carotid angiography was performed but was negative. In July 1968 she was referred to this hospital. A general neurological examination was negative. The visual function was normal. The optic discs were blurred and elevated 1 D and the retinal veins were engorged. Encephalographic examination did not indicate any brain tumour and she was discharged. In March 1969 the disc protrusion had increased to 3 D and small haemorrhages and exudates had appeared on the left disc. Therefore a new and extensive investigation was performed in this hospital. The ventricular fluid pressure was 10-20 mm Hg, i.e. slightly increased but neuro-roentgenological examinations were still negative. In spite of this, the progressive course supports the existence of an expanding intracranial lesion.

In 9 patients there was no papilloedema. The changes of the optic discs were either slight or typical of pseudo papilloedema. For examples, aged drusen in one disc existed in *case 1* myopia with supertraction and nasal blurring of both discs in *case 2* monocular hypermetropia with

From The Department of Ophthalmology, University Hospital, Lund, Sweden

DIFFERENTIATION OF PAPILLOEDEMA FROM PSEUDO PAPILLOEDEMA BY FLUORESCIN OPHTHALMOSCOPY

By

H G Bynke, M D and L Åberg, M D

The difficulties in differentiating between certain forms of papilloedema and pseudo papilloedema are well-known to ophthalmologists. This problem becomes urgent in cases where other symptoms are vague or absent, since the indication for an extensive neuro roentgenological examination is then entirely dependent on a correct interpretation of the disc changes.

According to Miller *et al* (1965), Jutte & Lemke (1968), Wessing (1968), and others, this differentiation may be facilitated by using fluorescein intravenously. As mentioned by David *et al* (1963) various abnormalities may be found by fluorescence technique in papilloedema. One of these is the 'residual' or 'deep' fluorescence of the optic discs. Thus, in papilloedema the dye leaks out through the vessel walls, producing a fluorescence of the extravascular tissue of the disc which may persist for hours. On the contrary, in pseudo papilloedema this fluorescence is lacking or very slight.

In 10 cases with papilloedema and 10 with pseudo papilloedema, which were reported by Miller *et al* (1965) there seem to have been no exceptions to this rule. Dollery *et al* (1965), who studied the disc fluorescence by quantitative methods, found that on an average, the intensity was significantly larger in oedematous than in normal discs. However, in 2 discs out of 23 with oedema it was of the same size as in 10 normal discs. The latter observation is of great clinical importance since the reliability of the method, among other things, must depend on the frequency of cases with true oedema, in which the fluorescence is so faint that the condition may be misinterpreted as pseudo oedema.

The present pilot study was performed in order to test the reliability of the method.

Material

The material consists of 25 patients, 13 male and 12 female, aged between 9 and 66 years (*Table*). Twenty three cases were treated as in

Table 1
Clinical data and results of fluorescein ophthalmoscopy in 16 cases with papilloedema and 9 with pseudo-papilloedema

Case No	Sex	Age (years)	Diagnosis	Type of disc change	Protrusion (Dioptres R E L E)		Other Qualities	Disc fluorescence	
								R.E	L.E
1	m	55	Parkinsonism	Pseudo-oedema	R.E	2 0	Drusen	0	0
2	m	21	Migraine	Pseudo-oedema		0 0	Myopia	0	0
3	f	66	Glioma frontal lobe	Oedema		<1 0	—	+	+
4	f	19	Syncope	Pseudo-oedema	R.E	<1 0	Constant findings 5 months	0	0
5	m	32	Cerebral contusion	Oedema		2 3	Haemorrhages	+	+
6	f	53	Carotid body tumour	Pseudo-oedema		<1 0	Constant findings 3 months	(+)	(+)
7	m	37	Art. hypertension	Oedema		2 2	Hypertensive retinopathy	+	+
8	f	48	Liquorrhea	Oedema		1 1	Regression some months	+	+
9	m	29	Subdural and intracerebral haematoma	Oedema		<1 <1	—	+	+
10	m	32	Jacksonian epilepsy	Pseudo-oedema		0 0	—	0	0
11	f	49	Cerebellar astrocytoma	Oedema		2 2	Regression 4 months	(+)	(+)
12	f	52	Glioma temporal lobe	Oedema		0 0	—	+	+
13	m	55	Glioma temporal lobe	Oedema		1 1	Haemorrhages	+	+
14	m	70	Post traumatic headache	Pseudo-oedema		1 1	Constant findings 2 months	(+)	(+)
15	f	43	Healthy	Pseudo-oedema		2 2	Constant findings 10 months	0	0
16	m	13	Epilepsy	Pseudo-oedema	R.E.	1 0	Hyperopia	R.E	0 (+)
17	f	33	Cerebellar astrocytoma	Oedema		3 3	Regression 2 months		
18	f	64	Acoustic neuroma	Oedema		1 2	Secondary atrophy	+	+
19	m	8	Art. hypertension	Oedema		3 2	Haemorrhages	+	+
20	m	9	Encephalitis	Oedema		3 1	Exudates	(+)	(+)
21	f	64	Meningeoma parietal lobe	Oedema		3 1	Regression 1 month	(+)	(+)
22	f	51	Intracranial hypertension	Oedema		2 2	—	+	+
23	m	40	Glioma frontal lobe	Oedema (slight)		3 3	Haemorrhages	+	+
24	f	33	Acoustic neuroma	Oedema		0 0	Exudates	+	+
25	m	47	Meningeoma parietal lobe	Oedema		0 0	Constant findings 2 months	(+)	(+)
						4 4	Macular oedema	(+)	(+)
						2,2	Haemorrhages	+	+

ipsilateral disc changes in *case 4* and constant disc changes over 10 months without subjective symptoms in *case 15*

Because of co existing general symptoms, neuro roentgenological examinations were performed in 4 patients with pseudo papilloedema (*cases 1, 4, 6 and 10*) but were negative. In one single patient (*case 23*) a brain tumour was discovered and verified by surgery before any ocular examination had been performed. The very slight, nasal blurring of the discs of that case was constant over 2 months and was interpreted as a normal finding.

To sum up, the diagnosis of the disc changes could be considered valid in all the cases on account of various clinical data and typical course.

Method

After a complete neuro-ophthalmological examination the patient was placed recumbent with his pupils dilated by Cyclogyl 1% (Schieffelin). Three ml. of Fluorescein sodium 20% (ACO) were rapidly injected into the cubital vein or into a vein of the dorsum of the hand. The time after the injection was recorded by a stop watch. The eye grounds were examined by means of a Zeiss Opton ophthalmoscope with a blue filter (BG₁₂) inserted, as described by Jutte & Lemke (1968). Through this filter the fluorescein appears as a greenish-yellow glow against the blue back ground.

Before the injection, the dark adapted observer examined the fundi to recognise their appearance in the blue light. Immediately after the injection the fundi were observed practically continuously during the first 5 minutes and then repeatedly with intervals of about 5 minutes until half an hour had passed.

No important complication of the injection was observed. However, 7 patients got nausea of short duration with or without vomiting. This appeared 1-2 minutes after the injection and disappeared about one minute later.

Observations

Between 10 and 20 seconds (av. 11) after the intravenous injection the dye appeared in the retinal arteries and a few seconds later in the veins. In this early phase it also filled out the superficial vascular plexus of the optic discs. This was dilated in several cases with papilloedema and became very conspicuous after the injection. During the following minutes the fluorescence of the retinal vessels gradually subsided. A choroidal fluorescence also became more or less apparent after some minutes.

Comments and Conclusions

In this study attention was mainly paid to the deep, residual fluorescence of the optic discs. This was found to be much more marked in 12 out of the 16 cases with papilloedema than in the 9 cases with pseudo-papilloedema. Therefore, the fluorescein examination seems to be valuable for a differentiation of the two conditions. This conclusion agrees with that of Miller *et al* (1965), Jütte & Lemke (1968), Wessing (1968), and others.

In 4 out of the 16 cases with oedema, the disc fluorescence was faint and of the same order of size as in some cases with pseudo-papilloedema. Consequently a 'negative result' does not exclude the possibility of papilloedema. In the case with the faintest fluorescence the papilloedema was of the chronic type. It should be mentioned that O Day *et al* (1967) found the deep fluorescence to be absent or reduced in optic atrophy and chronic papilloedema, respectively.

Sanders & Hytche (1967) reported characteristic changes after fluorescein injection in drusen of the disc. Such changes were not observed in the single case in this series in which drusen existed.

The disc fluorescence was found to appear about 1-2 minutes after the injection, reached a maximum after 10-15 minutes and persisted for at least half an hour. To recognise this phenomenon it may therefore be sufficient to start the fundus examination some minutes after the fluorescein injection. Furthermore, because of the reduced demand of timing, the complicated photographic device may be replaced by the handy ophthalmoscopic method as in this study. In a busy clinical routine, such simplifications are useful and may even be necessary.

Although a photographic method would be expected to permit a more objective quantification of the disc fluorescence, it should be pointed out that even that method is impaired by sources of error. One important error was mentioned by Lemke *et al* (1967): on the photograph the fluorescence before the injection (the primary fluorescence) cannot be distinguished from that due to fluorescein (the secondary fluorescence).

Summary

In 16 cases with papilloedema and 9 with pseudo-papilloedema the optic discs were studied by blue filter ophthalmoscopy after intravenous injection of fluorescein. The deep disc fluorescence was found to be much more marked in the majority of the cases with oedema than in the cases with pseudo-oedema. However, in 4 cases with oedema it was faint and of the same order of size as in some cases with pseudo-oedema.

It was concluded that fluorescein ophthalmoscopy is valuable for a differentiation of the two conditions but that the method is not entirely reliable.

In the cases with papilloedema, a diffuse fluorescence of the optic discs was first observed between $\frac{1}{2}$ and $2\frac{1}{2}$ minutes after the injection. It started on a small area and gradually extended over a larger part of the disc. In some cases the dye faded into the surrounding retina and after several minutes into the vitreous body. The intensity of the disc fluorescence gradually increased and reached a maximum about 10–15 minutes after the injection. At this point the dye had almost disappeared from the retinal vessels. It was observed only in the walls of some branches. This deep, residual disc fluorescence persisted at the end of the examination half an hour after the injection.

The intensity and extension of the disc fluorescence varied individually but was considerable in 12 of the 16 cases with oedema (*Table*). In some cases it was even larger than might be expected from the size of the oedema. For example, in *case 3*, in which there was an unmistakable but small oedema of the right disc but only a slight nasal blurring of the left, the fluorescence proved to be bright also in the left disc. Therefore, it was possible to conclude, on the basis of the fluorescein examination, that the papilloedema was bilateral.

In 4 cases with oedema the disc fluorescence was found to be faint. *Case 11* was the most remarkable one in this respect. Both discs were blurred around their margins, elevated 2 D and a little pale, but visual function was normal. There were multiple, refractile bodies on the disc surface. The retinal veins were engorged but there were no haemorrhages. Although a chronic papilloedema was suspected, a pseudo papilloedema seemed to be possible. The disc fluorescence proved to be very faint, so the condition might have been misinterpreted as a pseudo oedema. But there was also a pathological nystagmus. Therefore, a complete neuro-roentgenological examination was performed and showed a tumour in the posterior fossa. After the removal of a cerebellar astrocytoma the discs became normalized in the course of about four months, and the diagnosis of a true papilloedema could be confirmed. Also in *case 20*, the papilloedema was of the inveterate type, but the subjective symptoms had only lasted for about one month. In the other two patients with a faint fluorescence, *cases 19 and 24*, the oedema appeared to be of the recent type but without haemorrhages.

In the 9 cases with pseudo oedema, including *case 23*, the disc fluorescence was either lacking or very faint (*Table*). Furthermore, it was usually not observed as early after the injection as in the cases with papilloedema. No disc fluorescence was observed in *case 1*, in which there were buried drusen in the right disc. In *case 16*, in which the pseudo oedema was unilateral, a faint fluorescence was found only in the normal disc.

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UNILATERAL PAPILLOEDEMA IN NEUROSURGICAL PATIENTS

By

E Bruntse

In neurosurgical patients papilloedema usually is regarded as an expression of increased intracranial pressure. In spite of much research little is known about the pathogenesis of this papilloedema. Most theories regarding the formation of papilloedema are mechanical and are based on the fact, that the subarachnoid space of the brain and of the optic nerve are in connection with each other. If the intracranial pressure increases a corresponding increase will occur around the optic nerve. The central retinal artery and vein pass through the subarachnoid space just behind the eye. An increase of subarachnoidal pressure is believed to result in a compression of these vessels, the vein to a greater extent than the artery resulting in venous engorgement. The classic interpretation is that this venous engorgement is what causes papilloedema — choked disc. There is probably no doubt that the above mentioned conditions may have something to do with the development of papilloedema, but it is only part of the explanation. An essential objection is that venous engorgement would be expected to result in oedema of the retina rather than of the optic nerve head. The fact that even total obstruction of the central retinal vein rarely or never results in more than about three dioptries swelling is another important objection to the theory that venous engorgement should be the only factor in the pathogenesis of the oedema.

Parinaud's theory that it would be natural to regard the papilloedema merely as oedema in a part of the brain has principally been accepted by recent research workers. At present attention is being paid to the vessels which nourish the papilla, i.e. mainly branches from the circle of Zinn. Bregeat concludes in his book *L'Oedeme Papillaire* that the vascular changes which are found in the oedematous papilla are similar to vascular changes in other parts of oedematous brain tissue. He thinks that disturbances of circulation following these vascular changes are the cause of the oedema and that they moreover are due to disorder in a common regulation

REFERENCES

- David, N J, Heyman A and Hart L M* Fluorescence photography of retinal vessels and optic discs in papilloedema *Trans Am Neurol Ass* 88 (1963) 155-158
- Dollery, C T, Maier, C M and Hodge, J V* Studies by fluorescence photography of papilloedema in malignant hypertension *J Neurol Neurosurg Psychiat* 28 (1965) 241-246
- Jutte A and Lemke L* Intravitalfarbung am Augenhintergrund mit Fluorescein Natrium *Klin Monatsbl Augenh* Suppl 49 (1968) 128 pp
- Lemke, L, Tilgner S and Jutte, A* Fehlerquellen der Fluoreszenz Fotografie *Ophthalmologica* 153 (1967) 349-354
- Miller S J H, Sanders M D and ffytche, T J* Fluorescein fundus photography in the detection of early papilloedema and its differentiation from pseudo-papilloedema *Lancet* 3-4 (1965) 651-654
- O Day, D Crock, G and Galbraith, J E A* Fluorescein angiography of normal and atrophic optic discs *Lancet* 2 (1967) 224-226
- Sanders, M D and ffytche T J* Fluorescein angiography in the diagnosis of drusen of the disc *Trans Ophthal Soc U K* 87 (1967) 457-468
- Wessing, A* Fluoreszenzangiographie der Retina Stuttgart G Thieme (1968) 212 pp

cranial space occupying lesion regardless of place or type may result in occasional homo as well as contralateral papilloedema. Conclusions have been attempted drawn up on the basis of clinical experiences but apart from a few broad outlines it is difficult to find any essential agreement. Bregeat is of the opinion that cerebral abscess and temporal incarceration of the brain rather often have more papilloedema on the same side as the brain lesion than on the other. Tonnis' material of 111 intracranial tumours with unilateral papilloedema showed that tumour at the base of the brain as well as brain stem tumours often had homolateral papilloedema, while tumours of the occipital lobe comparatively often had contralateral. More records have been made on asymmetric papilloedema than on unilateral. Gibbs concludes on the basis of 330 cases of brain tumour with asymmetric papilloedema among other things (1) Greater choking tends to occur on the same side as the tumour (2) The incidence of homolaterally greater choking is highest among tumours of the temporal and parietal lobes (3) The incidence of contralaterally greater choking is highest among occipital tumours.

Paraicz *et al* and Dubansky *et al* have investigated several hundred patients with brain tumours and papilloedema. Among other things they have been interested in the asymmetric papilloedema. The former is of the opinion that pontocerebellar tumours often resulted in homolaterally greater choking. The latter finds that 75% of supratentorial tumours equally often resulted in contralaterally or homolaterally greater choking.

It appears then that the ophthalmologist often will find himself in a difficult situation when the neurosurgeon asks for an explanation of a unilateral papilloedema. This is the reason for us having taken an interest in examining the cases of unilateral papilloedema which we have had the opportunity to observe. We cannot expect other results from our examination than material for comparison. The patients were all admitted to the neurosurgical ward of the State Hospital in Copenhagen, and all eye examinations were carried out at the eye clinic of the same hospital. During a course of 15 years from 1954–1968 55 cases of unilateral papilloedema and probable intracranial disease were registered at the eye clinic. During the same period 1 291 patients suffering from bilateral papilloedema were examined i.e. 4.4% of the patients with papilloedema were found to have unilateral oedema. Perhaps a few of the 1 291 patients were not suffering from intracranial disease but it must have been only a few so even if the percentage is not precise it still shows something about the number of cases moreover it is in agreement with what others have found.

Among the 55 patients with unilateral papilloedema 27 had brain tumour, 4 had brain abscess, 4 had subarachnoid haemorrhage from an aneurysm, 9 patients had traumatic brain injury and 1 were found to have

mechanism Bregeat does not deprive mechanical factors in and around the optic nerve head all significance. Niedermeier points out more precisely the influence of these factors by suggesting that an increase in pressure in the subarachnoid space around the optic nerve may stimulate the sympathetic nervous system so that the vessels of the papilla are affected in such a way that it causes oedema. Bynke's stereophotographic investigations of pulse-synchronous level variations of the papilla of the optic nerve seem to agree with the conception, that papilloedema is caused by vascular disorders of the tissue.

However the oedema may be produced it would be natural to expect papilloedema due to increased intracranial pressure to become bilateral, and so it actually does in most cases. Swelling of the discs is often unequal. The oedema is rarely purely unilateral. Still it would be most natural to imagine, that the origin of asymmetric and unilateral oedema in most cases will be the same, only the releasing factors are more pronounced in unilateral cases. A great many of the asymmetric oedemas have no doubt been unilateral at first. None of the theories on the origin of choked disc exclude the possibility of unilateral oedema but do not on the other hand, provide any universal explanation of the unilaterality. From clinics a number of cases which were always unilateral are known. It is well-known that oedema hardly ever develops in an atrophic papilla or in a papilla that presents alterations which are characteristic of excessive axial myopia. It has long been known that any difference of the intraocular pressure on the two sides influences the development of papilloedema, hypertension restrains, hypotension promotes papilloedema. Here it seems to be local conditions that are of importance. Patients with Foster-Kennedy's syndrome, atrophy of one papilla and oedema of the other, make out a special group, characteristic of which it is that the atrophy as well as the oedema is due to intracranial disease. It is believed that in such cases, an interruption of the connection between the subarachnoid space of the brain and one of the optic nerves is of fundamental importance. Under these circumstances increased pressure in the subarachnoid space of the brain will only be able to reach the optic nerve head on one side.

When neurosurgical patients with unilateral papilloedema due to local conditions have been ruled out a small group remains with apparently inexplicable unilateral oedema. If the diagnosis of them moreover, is uncertain, one faces the problem whether unilateral papilloedema has any diagnostic value. This problem is often dismissed just by stating that it probably has not, although no one seems to be able to hide that this is a matter which little is known about.

Attempts have been made to solve the problem by clinical methods, but records available on the subject are sparse. According to these any intra-

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opticohiasmatic arachnoiditis No explanation as to the cause of the oedema was found in 4 cases The last patient was a child with congenital hydrocephalus A closer examination immediately showed that the unilateral papilloedema in 20 cases certainly was due to local conditions Exophthalmos, excessive myopia or a Foster-Kennedy syndrome was found In 6 cases the oedema was observed only after operation In 4 cases no signs of intracranial disease were found, all 4 patients had normal visual acuity and normal visual fields

Remaining are 25 patients with verified intracranial disease and unexplainable unilateral papilloedema 14 of these had cerebral tumour, 2 had brain abscess, 4 had intracranial haemorrhage caused by an aneurysm, the remaining 5 patients had traumatic cerebral injury

11 gliomas, 3 meningiomas, 2 abscesses, 1 intracranial haemorrhage and 3 traumatic injuries had caused homolateral papilloedema, which thus was found in 17 cases 14 of these various brain affections were located either in the frontal or in the temporal part of the brain 1 meningioma was found in the parietal lobe, another in the occipital lobe 1 subdural haematoma was inaccurately defined

2 gliomas, 3 aneurysms and 2 traumatic cerebral injuries had resulted in contralateral papilloedema, which thus had occurred in 7 cases 3 of these brain affections, 1 tumour and 2 traumatic injuries were located in the occipital lobe 2 of the aneurysms were found on the middle cerebral artery, 1 on the posterior cerebral artery The remaining tumour with unilateral papilloedema, an oligodendroglioma in the posterior and middle cranial fossa proved to have a suprasellar part with a large vessel surrounding the contralateral optic nerve, i.e., the papilloedema was probably homolateral

1 glioma of the cerebellar vermis could be placed neither in the group of homo — nor in the group with contralateral papilloedema It is remarkable that the whole material only contained one patient with cerebellar tumour and no patients at all suffering from a tumour of the brain stem It is also striking that not one single child had cerebral tumour and unilateral papilloedema Considering our few patients it may be incidental that the mentioned groups are not represented here But it seems natural to suppose that cases of unilateral papilloedema in which the oedema quickly becomes pronounced as in fossa posterior tumours, which are especially common for children, are rather rare

By examining the description of the ophthalmoscopic pictures one notices that the papilloedema usually was moderate with a swelling of 1-2 dioptres 1 frontal glioma and 1 frontal haemorrhage resulted in bilateral oedema before the patients were operated Postoperatively bilateral oedema was found in 3 of the patients, 2 of these had been operated for

glioma respectively in the occipital lobe and the temporal lobe, the third patient for abscess in the frontal lobe

Tonometry was not performed in any of the patients and none of them were known to have glaucoma. It is improbable that a difference of tension should have caused unilateral papilloedema in any of our patients although it is a possibility which cannot be ignored entirely.

Nor have the neurosurgical observations resulted in any explanation as to why the papilloedema of these patients became unilateral. Only one description mentions a thick tumour vessel as a possible explanation to a papilloedema on the same side.

There seems to be no points of resemblance whatever between the ventriculograms made. The highest measured spinal fluid pressure was 1100 — the lowest was 60 mm of water.

The material was also examined concerning the occurrence of brain oedema. Information about this might be of interest especially as a number of theories about the pathogenesis of choked disc relies upon the presence of brain oedema. This examination has not implied a dependable result. It was noticed in one third of the cases that the dura was under pressure or the brain oedematous at the beginning of the operation. In a few cases it was noticed that nothing remarkable appeared above cortex. According to the diagnosis there seems to be no doubt that most of our patients must have had brain oedema.

The present material is too small to allow for the drawing up of any conclusions whatsoever. It can only be stated that in the examined group of 25 patients suffering from unilateral papilloedema homolateral oedema was found in 17 cases, contralateral in 6. 2 patients with lesions in the middle of the brain had unilateral papilloedema.

15 out of 17 patients with homolateral papilloedema had lesions in the temporal or frontal lobe of the brain. Only 2 tumours in the posterior part of the brain had homolateral papilloedema. 3 out of 6 patients with contralateral papilloedema had affections of the occipital lobe. Thus one may agree with those who are of the opinion that as a rule greater choking of the disc tends to occur on the same side as the brain affection and that especially affections in the frontal part of the brain result in homolateral oedema while occipital lesions equally often result in contralateral oedema. Although unilateral papilloedema perhaps occurs with some regularity it still seems probable that for the neurosurgical diagnosis, unilateral papilloedema only exceptionally has greater value than bilateral.

Summary

During a course of 15 years, 55 patients suffering from unilateral papilloedema and probable intracranial disease were admitted to the neurosurgical ward of the State Hospital in Copenhagen. These patients were examined in order to determine whether the unilateral papilloedema had been or might have been of any significance for the neurosurgical diagnosis.

30 cases were immediately ruled out. 20 had unilateral papilloedema caused by local conditions, in 6 cases the oedema was diagnosed post-operatively, and in 4 cases no cause could be determined. The remaining 25 cases include 14 brain tumours, 2 abscesses, 4 intracranial haemorrhages caused by an aneurysm, and finally 5 patients with traumatic brain lesions.

17 of the 25 had homolateral, 7 had contralateral papilloedema. The last patient suffered from a midline tumour.

The examined material is too small to allow for the drawing up of any conclusions, but after having completed the examination, one may agree with those who are of the opinion, that as a rule there is most papilloedema on the same side as the brain affection, and that especially affections in the frontal and temporal part of the brain result in homolateral papilloedema, while occipital lesions just as often result in contralateral oedema.

REFERENCES

- 1 Bregeat P. L'Oedème Papillaire. Masson et Cie Editeurs. Paris 1957.
- 2 Bynke, Hans G. Puls-synkrona Nivåvariationer i Synneris papillen. Lund 1962.
- 3 Dubansky B et al. *Csl Oftal* 12: 334-40 1956 (cit. in *Ophthal Let*).
- 4 Gibbs F A. *Arch Neurol Psychiat* 27: 828-35 1932.
- 5 Glew W. *Am J Med Sci* 239: 221-30 1960.
- 6 Niedermeyer S. *Arch f Ophth* 57: 397-405 1955-56.
- 7 Paratcz F et al. *Psychiat Neur Psychol* 9: 14-19 1957.
- 8 Szapira, J et al. *J Med Lyon* 48/1118: 593-99 1967.
- 9 Tonnis W. *Ber Deut Ophth Ges* 59: 6-27 1955.

Discussion

U Krause (Uleåborg)

At the University Eye Hospital in Uleåborg we have attempted to analyse the degree of protrusion in papilloedema by stereophotogrammetric methods. We reckon that the degree of protrusion can be measured to an accuracy of 0.1 mm, possibly to 0.01 mm, by cutting the disc in slices of known thickness; we obtain a clear three-dimensional conception of the form of the disc. Follow-up investigations are possible and changes in the form of the disc can be registered. We expect that this procedure will have great clinical value.

From the University Eye Clinic Rigshospitalet Tagensvej Copenhagen
(Heads Professor B Lætz MD and H H Sedorff MD)

INCIDENCE OF SPONTANEOUS VENOUS PULSATION IN THE RETINA

By

S E Lorentzen

Spontaneous pulsation of the retinal veins is limited to one or more veins on the optic disc, with examination by ordinary direct ophthalmoscopy. The venous pulsation manifests itself as a slow narrowing of the vein caliber followed by a somewhat more rapid dilation to the width the vein displays during the longest period until another narrowing sets in. This form of pulsation thus differs from the arterial pulse wave.

Palpation of the radial pulse simultaneously with observation in the ophthalmoscope of the spontaneous venous pulsation on the optic disc reveals that the narrowing of the vein occurs immediately before the start of the radial pulse.

In the presence of choked disc no spontaneous pulsation occurs of the veins on the disc. *Baurmann* (1925) for instance, found no cases of spontaneous venous pulsation among 20 patients with choked disc. Within the past six months I have examined 10 patients with choked disc without finding spontaneous venous pulsation in any of these.

On examining patients suspicious ophthalmoscopically of choked disc it is therefore important to note whether or not venous pulsation is present. If not the question arises of the significance of this phenomenon as an indicator of choked disc. In other words: how often is spontaneous venous pulsation present — or absent — on the optic discs?

Various investigations have been reported in the literature concerning the incidence of spontaneous venous pulsation on the normal disc. Table 1 gives a review of these. The table shows that incidences ranging from 15 to 75 per cent have been found.

Material and Results

The series investigated consisted of healthy individuals examined as out patients. The majority were examined with a view to refraction, while some were subjected to a general health examination including the eyes.

Summary

During a course of 15 years, 55 patients suffering from unilateral papilloedema and probable intracranial disease were admitted to the neurosurgical ward of the State Hospital in Copenhagen. These patients were examined in order to determine whether the unilateral papilloedema had been or might have been of any significance for the neurosurgical diagnosis.

30 cases were immediately ruled out. 20 had unilateral papilloedema caused by local conditions, in 6 cases the oedema was diagnosed post-operatively, and in 4 cases no cause could be determined. The remaining 25 cases include 14 brain tumours, 2 abscesses, 4 intracranial haemorrhages caused by an aneurysm, and finally 5 patients with traumatic brain lesions.

17 of the 25 had homolateral, 7 had contralateral papilloedema. The last patient suffered from a midline tumour.

The examined material is too small to allow for the drawing up of any conclusions, but after having completed the examination, one may agree with those who are of the opinion, that as a rule there is most papilloedema on the same side as the brain affection, and that especially affections in the frontal and temporal part of the brain result in homolateral papilloedema, while occipital lesions just as often result in contralateral oedema.

REFERENCES

- 1 Bregat, P. L. Oedème Papillaire. Masson et Cie. Editeurs. Paris 1957.
- 2 Bynke, Hans G. Pulssynkrona Nivåvariationer i Synnervs papillen. Lund 1962.
- 3 Dubansky, B. et al. Csl Oftal 12: 334-40 1956 (cit. e. Ophthal. Let.).
- 4 Gibbs, F. A. Arch. Neurol. Psychiat. 27: 828-35 1932.
- 5 Glew, W. Am. J. Med. Sci. 239: 221-30 1960.
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- 7 Parascz, E. et al. Psychiat. Neur. Psychol. 9: 14-19 1957.
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Table 2

Incidence of spontaneous venous pulsation and mean intra-ocular tension in mm Hg in 172 subjects, divided into 10 year age groups

Age group	Males	Fe males	Males & Fe males	Spontaneous venous pulsation present				Ven ous puls ation absent	Mean intra-ocular pressure in mm Hg	
				Right eye	Left eye	Unilat	Bilat		Right	Left
10-19	9	13	22	18 82%	17 77%	3 14%	16 72%	3 14%	11.6	11.8
20-29	19	9	28	22 72%	19 67%	5 18%	18 64%	5 18%	12.4	12.5
30-39	4	1	5	12 92%	9 69%	3 23%	9 69%	1 8%	13.6	13.5
40-49	12	17	29	29 100%	18 62%	11 38%	18 62%	0 0%	12.6	12.6
50-59	12	26	38	31 82%	27 71%	4 11%	27 71%	7 18%	13.6	13.9
60-69	9	16	25	23 92%	22 88%	3 12%	21 84%	1 4%	14.1	14.3
70-79	3	14	17	15 88%	17 100%	2 12%	15 88%	0 0%	15.6	15.4
All	68	104	172	150 87%	129 75%	31 18%	124 72%	17 10%	13.3	13.4

Spontaneous venous pulsation present in 279 out of 344 eyes or 81%.

Absent venous pulsation 65 out of 344 eyes or 19%.

In 31 of the 172 subjects, or 18 per cent the spontaneous venous pulsation was present in one eye only while in 124, or 72 per cent it was bilateral. In 17 of the 172 subjects, or 10 per cent no spontaneous venous pulsation was observed.

Of all the 344 eyes 279 or 81 per cent showed spontaneous venous pulsation while 65 or 19 per cent displayed no such pulsation.

Table 3 illustrates the incidences of spontaneous venous pulsation within each sex separately to elucidate whether the incidence of this phenomenon differs for males and females.

The table shows a slightly higher incidence in the female group than in the male. Venous pulsation was absent in 12 per cent of the males and 9 per cent of the females while for the whole series it was 10 per cent as stated above.

Table 1
Review of the statements found in the literature concerning the incidence of spontaneous venous pulsation

Author	Year	Number of subjects examined	Spontaneous venous pulsation		Number of eyes examined	Spontaneous venous pulsation	
			Number of subjects	%		number of eyes	%
Lang & Barrett	1889				61	45	74%
Bailliant	1918	66	38	58%			
Wiat	1920	42			80	16	20%
Elliot	1922	100	46	46%	200	98	49%
Reis*	1932	123	21	16%			
Sobański	1936	80	32	40%			
Redslob	1946	180		75%			
Weinstein & Forgacs	1947	100	50	50%			
Schulte	1948	100		36%			
Lawatz	1962	277	205	74%			
Ford & Sarwar	1963	5006		14.7%			

* states himself that the figures are minimum figures

The series included no cases of ophthalmologic abnormalities or fairly grave refractive errors (refractions between + and - 3 D)

The subjects were examined in the sitting position by direct ophthalmoscopy in a half darkened room, using a luminous electric ophthalmoscope. Each eye was carefully examined for spontaneous venous pulsation on the optic disc

Ophthalmoscopy was followed by slit lamp examination, and the tension of each eye was measured with an applanation tonometer

The investigation comprised 172 subjects (314 eyes), 68 males and 104 females ranging in age from 10 to 79 years

The results are shown in table 2, where the series has been divided into 10 year age groups. This table also gives the mean intra ocular tensions of the right and the left eye within each age group, as well as those of the right and the left eye in the total series. It is seen that spontaneous venous pulsation was present in 150 of the 172 right eyes (87 per cent) and in 129 of the 172 left eyes (75 per cent)

slightly above the intra ocular pressure, because the intravenous pressure is to support the intra-ocular pressure without the veins collapsing. In addition to secure the centrally directed venous blood flow a certain fall of the pressure towards the centre must take place. During the systole of the heart the intra ocular pressure rises 0.5–2 mm Hg, a rise noticed daily by applanation tonometry. If during the systole the intra ocular pressure rises to a certain level above the venous pressure the walls of the vein will be compressed, in part or entirely, with a consequent spontaneous venous pulsation. As stated above, this is only observed on the optic disc where it often is particularly pronounced at the site where the vein trunk dives into the vascular funnel.

Two explanations may be given of the fact that such a pronounced spontaneous venous pulsation as to be visible in the ophthalmoscope is only present on the optic disc. One is that the venous pressure is the lowest on the disc, and the other that the venules (and the arterioles) lie loose in the disc tissue being thus easily influenced by alterations of the intra ocular pressure with consequent variations in calibre. In the nerve fibre layer the retinal vessels on the other hand lie supported and stabilized by surrounding tissue. *Bailliant* as early as 1918 called attention to this fact which has since been borne out by *Schulze* (1948) on the basis of histological examinations.

The lower pressure in the venules on the optic disc than in those of the remaining retina has various causes. As stated above a minor fall of the venular pressure takes place in the central direction. This fall is further accentuated in the disc region the venules passing in this place from the higher intra-ocular pressure to the lower intraneural and later the intra orbital pressure. The so called Venturi effect plays a part as another cause of the lower venular pressure on the optic disc. When a liquid in a tube passes from one section of a fairly large caliber to another of a smaller caliber the flow rate increases with a consequent fall of the pressure. This is what happens on the optic disc the aggregate number of veins in the retina having a total diameter exceeding that of the few veins on the disc.

These facts in connection with the balance between the intravenous and the intra ocular pressure constitute the basis of the spontaneous venous pulsation which thus can be regarded as an ophthalmoscopic visible sign of the pressure fall in the veins of the optic disc region.

The present investigation gave the result that spontaneous venous pulsation on the optic disc was present in 81 per cent of all the eyes and 90 per cent of all the subjects (being unilateral in 18 per cent and bilateral in 72 per cent) between the ages of 10 and 79. Spontaneous venous pulsation was found to be absent in 10 per cent of normals.

Table 3
Incidence of spontaneous venous pulsation for 68 males and 104 females

Age group	Males					Females				
	Venous pulsation present		Venous pulsation absent			Venous pulsation present		Venous pulsation absent		
	Right	Left	Uni lat	Bi lat		Right	Left	Uni lat	Bi lat	
10-19	7	7	2	6	1	11	10	1	10	2
20-29	17	14	5	13	1	5	5		5	4
30-39	4	2	2	2		8	7	1	7	1
40-49	12	4	8	4		17	14	3	14	
50-59	7	5	2	5	5	24	22	2	22	2
60-69	7	7	2	6	1	16	15	1	15	
70-79	2	3	1	2		13	14	1	13	
All	56	42	22	38	8	94	87	9	86	9
%	82%	62%	32%	56%	12%	90%	84%	9%	82%	9%

As seen in the table 2, the incidence of spontaneous venous pulsation showed a tendency towards a minor rise in the two oldest age groups

The mean intra-ocular pressure was 13.3 mm Hg for the total series (344 eyes). As might be expected, the intra ocular pressure, with a single exception, rose steadily from 11.7 mm Hg in the 10-19 year age group to 15.5 mm Hg in the 70-79 year group

The 279 eyes with spontaneous venous pulsation had a mean intra ocular pressure of 13.4 mm Hg, and the 65 eyes with no such pulsation a mean pressure of 12.8 mm Hg

The mean intra ocular pressure was the same for the males and females of this series, namely 13.3 mm Hg, calculated as the mean for 136 male and 208 female eyes respectively

Discussion

This paper is only concerned with the incidence. It was not intended to investigate the numerous factors which may possibly underlie the occurrence of spontaneous venous pulsation in the retina. Thus, for instance, the humoral blood pressure was not measured, nor was any attempt made to estimate the pressure in the retinal veins by ophthalmodynamometry. Nevertheless it seems reasonable to mention some of the factors influencing the occurrence of spontaneous venous pulsation.

The retinal vein pressure is supposed to be on a level with, and usually

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OSTEOPETROSIS FROM THE OPHTHALMOLOGICAL POINT OF VIEW A REPORT OF TWO CASES

By

Henry Aarset

Osteopetrosis (Harshner 1926) is a descriptive name given to a disease previously known by various other names including Albers Schonberg's disease osteosclerosis fragilis generalisata, osteosclerosis congenita diffusa

It is a rare disease causing an abnormal skeletal development. The osteoclastic activity normally observed as a part of the moulding process is inadequate in these patients. The primarily mineralised bone tissue is not removed with normal speed, while the formation of new bone is unimpaired (Zetterstrom 1957). This results in generalized thickness of the compact bones, narrowing of the marrow cavities and secondary sclerosis of the bone tissue.

The cause of the disease is not known. It is evident however that it is frequently hereditary. The sexes seem to be equally affected and no racial preponderance has been demonstrated. The disease was first recognized in live patients in 1904 (Albers Schonberg). It has been classified into four different types based on clinical and geneal observations (Schinz 1952).

Type 1 Genetically dominant clinically benign

Type 2 Genetically dominant, clinically benign in the early stages later malignant

Type 3 Genetically recessive clinically benign

Type 4 Genetically recessive, clinically malignant

The benign types whether caused by dominant or recessive traits may be discovered by chance at any age on routine X ray examination. These types do not show any particular ophthalmological manifestations.

Type 2 is a rare dominant form which may be benign initially but later runs a malignant course with development of a severe anaemia and optic atrophy as in type 4 (Schinz 1952).

The malignant autosomal recessive type of the disease has the greatest ophthalmological interest. It gives clinical symptoms from the first

REFERENCES

- Baillart, P* La circulation veineuse rétinienne *Annal d'Oculist* 1918, 15, 453-472
- Baurmann, Max* Ueber die Entstehung und klinische Bedeutung des Netzhautvenenpulses Bericht 45 Zusammenkunft Deutsch Ophthal Gesellsch 1925 J F Bergmann Munchen 1925, p 53-59
- Elliot, R H* The retinal pulse *Brit J Ophthal* 1921, 5 481-500
- Ford, M and Sarwar, M* Features of a clinically normal optic disc *Brit J Ophthal* 1963 47 50-52
- Lang W and Barrett, James W* On the frequency of cilio retinal vessels and of pulsating veins London *Ophthal Hosp Rep* 1889, 12 59-60
- Lauwitz, B* Om stasepapillers patogenese og diagnose *Dansk Oftalmologisk Selskabs* 375 møde Nyborg Strand April 1962
- Redslob, E* Valeur de la pression veineuse rétinienne *Annal d'Oculist* 1946, 179 367-374
- Reis, Wiktor* Der Netzhautvenenpuls und der intrakranielle Druck *Zeitschr f Augenheilk* 1932 78 47-54
- Schulte, D* Gefassstudien mit Augenspiegel und Spaltlampe I Mitteilung Beobachtungen uber den Netzhautvenenpuls *Klin Mbl Augenheilk* 1948, 113 220-230
- Sobanski, J* Der Blutkreislauf in der Netzhaut unter physiologischen Bedingungen *Archiv f Ophthalmologie* 1936 135 372-382
- Weinstein, P and Forgedes J* Circulatory studies of the fundus of the eye *Brit J Ophthal* 1947, 31 238-243
- Wiart, Louis* Contribution à l'étude du pouls veineux rétinien Librairie littéraire et médicale Louis Arnette, Paris 1920

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Type 2 is a rare dominant form which may be benign initially but later runs a malignant course with development of a severe anaemia and optic atrophy as in type 4 (Schinz 1952).

The malignant autosomal recessive type of the disease has the greatest ophthalmological interest. It gives clinical symptoms from the first

months of life. It has even been demonstrated in utero by X ray examinations (Pirie 1930)

The bone changes causes an increased fracture tendency

The effect on the bone marrow leads to extra medullary blood formation with subsequent hepato splenomegally and generalized lymphadenopathy. The important haematological changes are haemolytic anaemia and thrombocytopenia. Immature myeloid cells and nucleated erythrocytes can be demonstrated in the peripheral blood.

The anaemia is due to increased haemolysis in the reticuloendothelial system. The spleen has been shown to be the principle site of destruction (Engfeldt *et al* 1955, Sjolín 1959)

The ophthalmological and neuro ophthalmological findings are secondary to changes in the cranium

Hydrocephalus is frequently reported but papilloedema has only been observed in one case (Laurell & Wallgren 1920)

Deformities of the orbit and maxilla may lead to exophthalmus (Malatesta 1954, Pietruschka 1953 and 1958, Sjolín 1959, Ellis & Jackson 1962, and others). Narrowing of the foramina at the base of the skull may lead to lesions of the cranial nerves causing squint, ptosis, anisocoria and paralysis of the facial muscles (Pietruschka 1953 and 1958, Sjolín 1959, Ellis & Jackson 1962, Hill & Charlton 1965, and others)

Nystagmus occurs frequently and it is probably of ocular origin

Optic atrophy is the commonest and most serious ophthalmological lesion. It is due to compression of the optic nerve and blood vessels in the narrowed optic canal (Pirie 1930, Riser 1941, Wheeler 1946, Eggert 1947, Sundal 1951, Pietruschka 1958, Malatesta 1954, Sjolín 1959, Modi & Kandoth 1964, Dent *et al* 1965, Ellis & Jackson 1962, Hill & Charlton 1965, Anand 1966, Morrow *et al* 1967, Farniaux *et al* 1967, Baird *et al* 1968, and others)

This malignant type has a very bad prognosis. Death often occurs within the first year of life.

The treatment of malignant osteopetrosis is often disappointing. The anaemia and thrombocytopenia are in some cases improved by splenectomy (Sjolín 1959, Moe & Skjæveland 1969). Corticosteroid therapy has been tried with variable effect (Dent *et al* 1965, Farniaux *et al* 1967, Moe & Skjæveland 1969)

To prevent progressive atrophy of the optic nerve, decompression of the optic canal is recommended (Ellis & Jackson 1962, Hill & Charlton 1965)

Case reports

Two cases suffering from the autosomal recessive type of malignant osteopetrosis have been treated in the Department of Pediatrics, University of Bergen, since 1967. They are described in more detail in another publication, particularly with regard to therapy (Moe & Sjøaevland 1969).

Case 1 Female born March 1967. Birth weight 2 490 gr. Length 49 cm. Admitted to the Department of Pediatrics at the age of 2½ months. Findings on admittance: Enlarged liver and spleen, anaemia and thrombocytopenia. Lab tests: Hb 9.1 gr pr 100 ml, WBC 18 400 pr cmm. Blood film showed immature myeloid cells and nucleated red cells. Reticulocytes 120 per thousand, thrombocytes 40 000 pr cmm. Serum calcium 7.9 gr pr 100 ml, Serum phosphorus 2.9 mg pr 100 ml, Serum bilirubin 0.5 mg pr 100 ml and serum haptoglobin 7 mg pr 100 ml.

There was evidence of increased red cell destruction in the liver and spleen.

Ophthalmological examination at the age of 3 months revealed no abnormalities. When the child was 8 months old a left-sided concomitant converging squint was recorded. The discs were at this time pale with sharp borders identical with those seen in bilateral primary optic atrophy. The direct light pupillary reflex was normal on the right side but doubtful in the left eye.

From the age of about 2½ months the patient has been treated almost continuously with Prednisone. The maintenance dose (10 mg) was given on alternate days. This resulted in a normalisation of the haematological picture and a satisfactory general development of the child.

Though relatively good general condition, signs of optic atrophy without gross deterioration of vision were regarded as indications for neuro-surgical treatment. Decompression of the right optic canal was performed in the hope of preventing further progression of the optic lesion. The operation was undertaken in March 1968 through a right frontal flap. A marked thickening of the orbital roof and narrowing of the trabecular space was noted. Histological examination of the removed bone showed scattered haemopoietic foci.

Postoperative progress was uncomplicated. A year and a half after the operation the vision on the right eye is still good. She walks about without difficulty. The vision on the left eye is probably limited to light perception.

Case 2 Male born July 1967. Birth weight 1900 gr. Length 48-49 cm. Periods of fever from the age of 3½ months. Admitted to Department of Pediatrics when 5 months old. On admittance he was small and pale, weight 4.7 kg, length 59 cm. The anterior fontanelle was slightly bulging. Head circumference was normal. There was marked hepatosplenomegaly, general lymphadenopathy, haemolytic anaemia and thrombocytopenia. Lab tests: Hb 7.8 gr pr 100 ml, WBC 33 000 pr cmm. Peripheral blood film showed immature myeloid cells and nucleated red cells. Reticulocytes 100 per thousand, thrombocytes 30 000 pr cmm. Serum calcium 8.7-6.9 mg pr 100 ml, Serum iron 1.2 microgr pr 100 ml, Serum bilirubin 0.4 mg pr 100 ml and serum haptoglobin 0 mg pr 100 ml.

The life-span of the red cells was reduced and the spleen was the main site of destruction.

This patient was in a poorer general condition than case 1. He also came under medical care at a later stage. Persistent treatment with high doses of Prednisone failed to produce complete normalisation of the blood picture. Splenectomy was undertaken.

in the end of January 1968. Subsequently it was possible to reduce the steroid dosage and it was stabilized on 15 mg every other day. The blood picture has later remained satisfactory, even though some degree of haemolysis and thrombocytopenia have persisted.

Ophthalmological examination showed a variable divergent squint and an irregular ocular nystagmus. The right pupil showed an *indefinite* reaction to light, while the left eye showed an amaurotic reaction. There was a marked optic atrophy with pale discs in both eyes. Vision was probably *restricted* to light perception in the right eye and amaurosis in the left eye.

Owing to the poor general condition and the poor visual function in this patient, decompression of the optic canal was not undertaken.

The diagnosis was confirmed in both cases by typical X-ray changes with generalized osteosclerosis, thickening of the compact bone, lack of differentiation of the compact bone and marrow together with rachitic like appearance of the epiphyses (fig 1, 2 and 3).

Following Prednisone therapy there was an improvement in the rachitic like changes but not in the osteosclerosis.

Both case 1 and 2 were the only children of healthy, non-related parents.

Two other cases with the same disease have been published previously from the Department of Pediatrics, University of Bergen (Sundal 1951). They were brother and sister with healthy parents and two healthy siblings. Both the affected children had seizures, hepatosplenomegaly and anaemia. Ophthalmological examination was only carried out in one of them revealing optic atrophy. One received no treatment, the other received several blood transfusions. Both died at the age of 5 months.

Commentary

Atrophy of the optic nerve is the most common and the most serious ophthalmological manifestation of the malignant, autosomal recessive type of osteopetrosis.

In the majority of cases the clinical picture is dominated by serious general symptoms. The fact that the ultimate prognosis is very poor explains why the ophthalmological symptoms tend to be understressed. Blindness is however, a very real threat to those patients who survive the early childhood years.

A minority of cases presents with ophthalmological symptoms and may be referred to the ophthalmologist as a case of poor vision or squint (Hill & Charlton 1965).

The optic lesion is due to compression of the optic nerve in the optic canal. Decompression of this canal may be performed. In the literature there are records of three patients with osteopetrosis who have been subjected to this operation. One patient had only doubtful light perception left before the operation, and no improvement could be demonstrated following surgery (Hill & Charlton 1965). Two other cases are recorded where vision is described as good even two years after the operation (Ellis & Jackson 1962, Hill & Charlton 1965).



Fig. 1
Roentgenograms of skull in osteopetrosis showing marked sclerosis in comparison to a normal skull (left)

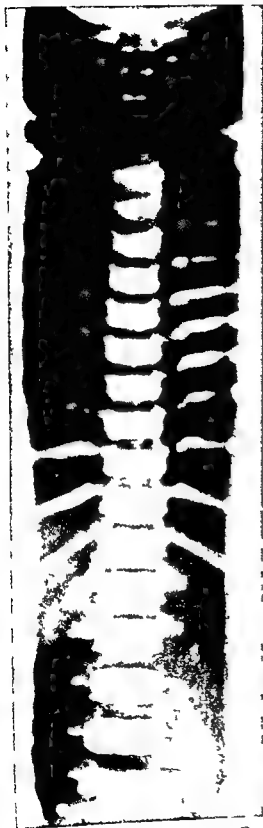


Fig 2 and 3
Roentgenograms of spine and long bones showing marked sclerosis

One would therefore advocate surgical treatment in the cases where vision is good and where the general condition is satisfactory. With these views in mind decompression of the optic canal was carried out in one of our cases (case 1). Vision is still good on the treated side a year and a half after the operation.

Prednisone therapy has so far successfully checked the anaemia and the thrombocytopenia in the two reported cases. The steroid treatment is probably the main reason why the children are still alive.

Summary

Two cases of malignant genetically recessive type of osteopetrosis are described. The anaemia and thrombocytopenia have so far responded successfully to Prednisone therapy. Both cases showed primary optic atrophy presumably due to narrowing of the optic canals. One case presented with good vision in one eye and decompression of the optic canal was undertaken. The other case presented with very poor vision and surgery was considered to have little or nothing to offer.

Acknowledgements

I am indebted to P. J. Moc, M.D. for his permission to publish these two cases from the ophthalmological point of view.

REFERENCES

- Albers-Schönberg H. Röntgenbilder einer seltenen Knochenkrankung. *München med Wchr* 51 (1904) 365.
- Arand J S. Osteopetrosis (Albers-Schönberg's disease). Report of three cases in one Sibship. *Indian J Pediatr* 33 (1966) 177-181.
- Baird P A, Robinson G C, Hardwick D F and Sovereign A E. Congenital osteopetrosis. An unusual Cause of Hydrocephalus. *Canad Med Ass J* 98 (1968) 362-365.
- Dent C E, Smellie J M and Watson L. Studies in osteopetrosis. *Arch Dis Child* 40 (1965) 7-15.
- Egger H. Ein weiterer Fall von Opticusatrophie bei Marmor-Knochenkrankheit (Albers-Schönberg). *Klin Wbl Augenheilk* 112 (1947) 66-70.
- Ellis PA P and Jackson W E. Osteopetrosis. A clinical study of optic nerve involvement. *Amer J Ophthalm* 53 (1962) 943-953.
- Engfeldt B, Karlberg P and Zetterstrom, R. Studies on skeletal changes and on the etiology of the anemia in osteopetrosis. *Acta Pathol & Microbiol Scand* 36 (1955) 10-20.
- Farriaux J P, Willems M, Maillard E, Francois P and Fontaine G. La maladie d'Albers-Schönberg. Deux observations dans une fratrie. Considérations physiopathologiques. *Presse Med* 75 (1967) 705-710.
- Hill B M and Charlton H S. Albers-Schönberg disease. *Med. J. Aust.* 2 (1965) 363-367.
- Karlner R G. Osteopetrosis. *Amer J Roentgenol* 16 (1926) 403-419.

- Laurell, H and Wallgren, A Untersuchungen über einen Fall einer eigenartigen Skeletterkrankung (osteosclerosis fragilis generalisata) Uppsala Lakarf Forh 25 (1920) 309 Abst JAMA 76 (1921) 560
- Malatesta C Sopra un caso di malattia di Albers Schonberg Boll Oculist 33 (1954) 11-16
- Modi, P J and Kandath, W A Marble bone disease Case report with a review of the literature J Postgrad Med 10 (1964) 69-74
- Moe P J and Skjaereland A Studies in osteopetrosis Report of 4 cases In press in Acta Paediat Scand 1969
- Morrow, G, Barness, L A and Rasmussen, H Calcium Mobilization in osteopetrosis Amer J Dis Child 114 (1967) 161-167
- Pietruschka G Über Marmorknochenkrankheit (Albers Schonbergsche Krankheit) nebst Bemerkungen zu Differentialdiagnose Klin Mbl Augenheilk 123 (1953) 189-201
- Pietruschka G Weitere Mitteilungen über die Marmorknochenkrankheit (Albers Schonbergsche Krankheit) nebst Bemerkungen zur Differentialdiagnose Klin Mbl Augenheilk 132 (1958) 509-525
- Pitts A H Development of marble bones Amer J Roentgenol 24 (1930) 147-153
- Riser R O Marble bones and optic atrophy Amer J Ophthal 24 (1941) 874-878
- Schinz H R Lehrbuch der Röntgendiagnostik Thieme, Stuttgart 1952 664-677
- Sjolin, S Studies on osteopetrosis II Investigations concerning the nature of anemia Acta Paediat Scand 48 (1959) 529-544
- Sundal, A Osteopetrosis Clinical and post mortem examination of two cases Acta Paediat Scand Suppl 83 (1951) 83-86
- Wheeler, J N A case of osteopetrosis (Albers Schonberg as described in 1904) Trans ophtal Soc U K 66 (1946) 619-625
- Zetterstrom, R Osteopetrosis (Marble Bone Disease) Clinical and Pathological Review Mod Probl Paediat 3 (1957) 488-508

From The Department of Ophthalmology University of Bergen, Norway
(Head Professor dr med. Torstein Bertelsen)

OPERATIVE TREATMENT OF PARALYTIC STRABISMUS

By

Magnus Odland

The purpose of this paper is to give a report of some cases operated on for paralytic strabismus where muscle transplantations have been used. Transplantation of extraocular muscles has not been too generally practised. The most common procedure in management of the paralytic type of strabismus is to weaken the direct antagonist by recession of the muscle or of the contralateral synergist. If the paralysis is due to a lesion of the muscle itself, an operation to strengthen the affected muscle by resection or tucking is indicated and is often done together with a weakening operation of the direct antagonist.

Hummelsheim (1908) reported of having done transplantation as a treatment of paralysis of the lateral rectus muscle with good result. He isolated the outer halves of the superior and inferior recti muscles and transplanted them to the upper and lower edges of the lateral rectus muscle in order to augment the action. A number of modifications of the original technique have later been employed. O'Connor (1935) describes several types of operations not only for treatment of a lateral rectus muscle paralysis but also where there have been paralysis of other muscles such as superior rectus and medial rectus. One method he suggested for lateral rectus muscle paralysis was to transplant the medial thirds of the vertical recti in order to reduce the adduction action of these muscles. He also tried to transplant the vertical recti *in toto*. Hildreth (1953) tried to obtain abduction by shifting the direction of the vertical recti muscles by approximating them by means of a loop placed temporarily. The results reported with the different methods applied have varied considerably.

Own material

The routine management of paralytic squint at the eye clinic Haukeland Hospital is the above mentioned procedure of recession and resection. In most of the cases we get good results from these operations. Sometimes however, this is not so particularly in cases of complete

Table 1
Results of muscle transplantations on 10 eyes with lateral rectus muscle paralysis

Case	Age	Cause of paralysis	Deviation before operation	Abduction before operation	Duration of paralysis	Operation	Deviation after operation	Abduction after operation
Case 1	30	Skull fracture	Ca +15	Ca 30	21 months	Recession of R M R and transplantation (2 stages)	0	35°
Case 2	33	Congenital	Ca + 5	Ca 5°	28 years	Recession of R M R and transplantation (2 stages)	-6 exotropia +8	15°
Case 3	23	Encephalo pathia	+18	14	10 years	Transplantation	esotropia 0	18°
Case 4	54	Brain tumor (cordom)	+23	15	2 years	Recession of L M R and transplantation (2 stages)	0	11
Case 5	61	Skull fracture	Rt eye +25 Lt eye +50	5 0	11½ years "	Recession of R M R and transplantation (1 stage) Recession of L M R and transplantation (1 stage)	-5 exophoria +3	25° 5
Case 6	10	Skull fracture	+15	15°	8 months	Recession of both M R and transplantation (2 stages)	esophoria +4	19
Case 7	71	Skull fracture	+27	10	10 months	Recession of R M R and transplantation (1 stage)	esophoria 0	12°
Case 8	20	Concussion	+13	18	16 months	Recession of L M R and transplantation (1 stage)	0	27°
Case 9	14½	Congenital	+ 7	5	14½ years	Recession of L M R and transplantation (2 stages)	+5 esophoria	10

paralysis of the muscle, or if a marked contracture of the direct antagonist has taken place

During the last 11 years 12 patients have been operated on for paralytic strabismus by muscle transplantation. In 2 of the cases the operation was bilateral. 9 patients had the Hummelsheim operation done for lateral rectus paralysis, one of these was bilateral. 1 patient with a medial rectus muscle paralysis was operated on, and 2 patients had muscle transplantation done for superior rectus muscle paralysis. In one of the latter the operation was performed on both eyes.

The technique described by Stallard (1950) was applied on those cases who had paralysis of the lateral rectus muscle. The superior and inferior recti muscles are split along the axis of the muscle fibres for about 12 mm. Between one third to one half of the muscle is separated on the temporal side. The strips are then sutured through buttonholes to the lateral rectus at its insertion. On all these patients except one, recession of the medial rectus was done. In 5 patients this was done prior to the transplantation. On all other patients it was done together with transplantation in one stage. The data and results concerning these patients are shown in the table. Except for one patient (case 2) all had a compensatory head posture with the head turned in the direction of the affected muscle. After operation this symptom disappeared except in case 3 who still had slight deviation to the left paretic side but this did not cause him any trouble. Cases 4, 5 and 7 experienced diplopia in periods after the operation when looking straight forward but they were not bothered with it. Almost every patient noticed some degree of diplopia when turning the gaze in the direction of the paralyzed muscle. Fig. 1 shows the compensatory head posture in case 1 before operation and the abduction gained after operation (Fig. 2). The Hess screen tests are shown on Fig. 3 and Fig. 4. Fig. 5 shows his field of binocular fixation before and after the operation. Case 5 had considerable contracture of the medial recti as shown in Fig. 6. This man had an accident 11 years ago and got a bilateral abducens paralysis. The right eye had only slight movement to each side and the left eye was fixed in a maximal adducted position. In order to see straight he had to turn his head about 20 degrees to the right. Fig. 7 shows the result of the operation. He had only slight double vision in periods.

The one patient who was operated on for medial rectus muscle paralysis was a 23 year old man. In 1956 he had a resection done of the medial rectus muscle and also recession of the lateral rectus muscle. By examination in August 1968 there was still 15 degrees divergence and he was able to adduct the eye only to the midline. A muscle transplantation was then performed and the inner thirds of the vertical recti muscles were transplanted to the insertion of the medial rectus. There was however little

Table 1
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Case 5	61	Skull fracture	Rt eye +25 Lt eye +50	5 0	11½ years	Recession of R M R and transplantation (1 stage) Recession of L M R and transplantation (1 stage)	-5 +3	25° 5
Case 6	10	Skull fracture	+15	15	8 months	Recession of both M R and transplantation (2 stages)	+4	19
Case 7	71	Skull fracture	+27	10	10 months	Recession of R M R and transplantation (1 stage)	0	12
Case 8	20	Concussion	+13	18	16 months	Recession of L M R and transplantation (1 stage)	0	27
Case 9	14½	Congenital	+ 7	5	14½ years	Recession of L M R and transplantation (2 stages)	+5	10
							esophoria	

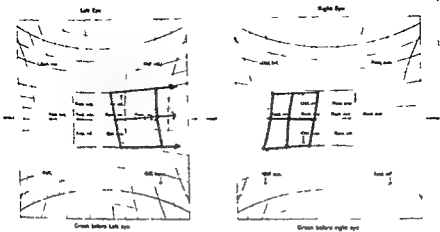


Fig 3
Case 1 Hess screen before operation

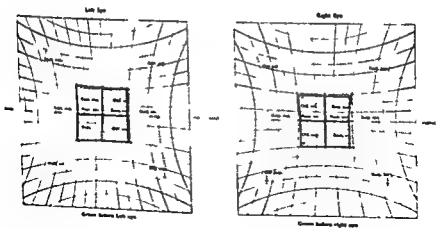


Fig 4
Case 1 Hess screen after operation



Fig 1

Case 1 Compensatory head posture in R lat rectus paralysis



Fig 2

Case 1 Abduction gained after muscle transplantation



Fig 6



Case 5 Marked contracture of the medial recti after bilateral abducens paralysis



Fig 7

Case 5 Eyes are straight after muscle transplantation

FIELD OF BINOCULAR FIXATION

 BEFORE OPERATION
 AFTER OPERATION

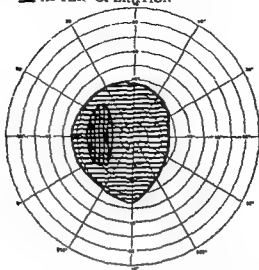


Fig 5

Case 1 Binocular field of fixation before and after operation

improvement In May 1969 a new resection and recession was done After this operation the eyes were almost straight in the primary position, but little adduction was gained He had no binocular function As already mentioned we also operated on 2 patients for defective elevation A 27-years old woman had an accident when she was 3 years old, and since then she was bothered with double vision This she compensated by abnormal head posture On examination in 1967 the left eye had 15 degrees convergence and a hypotropia of 8 prism diopters She could not elevate the eye above the midline In September 1967 she had a muscle transplantation done, and a strip from each of the medial and lateral recti muscles were moved to the insertion of the superior rectus, and the medial rectus was recessed After this operation she got hypertropia of the same eye About a year later the inferior rectus muscle was resected, and since there also was 13 degrees convergence, the same procedure was performed on the lateral rectus This gave a satisfactory result, and the diplopia disappeared

The other case with defective elevation was a 4 years old girl (Fig 8) The condition was congenital, bilateral and she also had ptosis As seen on the figure the head posture was grotesque She had first an operation for ptosis by Friedenwalds technique Afterwards muscle transplantation was performed with the same technique as described above As seen on Fig 9 there was no longer compensatory head posture She was able to elevate the eye 5-10 degrees above midline, but there was still a slight degree of ptosis left

Discussion

As to the time when surgery should be done on an acquired paralytic strabismus different views are held. Some surgeons (O Connor 1935 and Gifford 1940) feel that if there is no improvement of the paralysis after 3 months, the prospect of spontaneous cure is too slight to warrant much more delay because of danger of contracture. Others (Spach 1953 and Unve 1968) think that a period of at least a year should be allowed to elapse before operative treatment should be considered. A careful examination of the ocular movements, measurement of the angle of deviation in various directions of gaze, examination on the Hess screen or its equivalent and an assessment of the state of binocular function is necessary to follow the development of a possible onset of contracture or improvement.

Congenital ocular paralysis should be operated on early, at least where the strabismus is compensated by abnormal head posture in order to avoid structural changes in the cervical column.

Complications following muscle transplantations are rare. Stocchi and Bianchi (1957) and Girard and McNeely (1958) reported observing subacute iridocyclitis in a few patients in whom this operation had been done on a lateral rectus muscle paralysis. All four recti muscles had been operated on in one stage. Forbes (1959) reported a case which developed keratitis and the patient got an irregular pupil. The complication was thought to be due to ischemia of the anterior segment of the eye. This may be interpreted as a recommendation for two stage operation. We did not see any complications in our patients, not even in those who had the operation done in one stage.

Many are afraid to operate on an eye with a muscle paralysis, especially where there is a certain degree of deviation, because of the risk of developing diplopia or make a persistent diplopia more annoying. The reason for this should be that it is more easy to suppress a peripheral image than a central one. If the binocular function, however, is well preserved, or one is able to stimulate the fusional power, the chances for gaining a satisfactory result are good. Also if the paralysis has lasted for a long time, even grown up people may be able to suppress one image to a certain degree so that they will not be bothered by double vision if there is a rest deviation left. Prism glasses may be indicated if diplopia persists.

Summary

The most common way of treating paralysis of the external ocular muscles operatively is to weaken the direct antagonist or the contralateral synergist or both by recession of the muscles, if there still is left some



Fig 8

Grotesque compensatory head posture caused by bilateral superior recti paralysis and ptosis



Fig 9

Normal head posture gained after muscle transplantation and operation for ptosis

From The Department of Ophthalmology Ullevål sykehus University of Oslo
Norway
Head Professor dr med Jan Iltisborg

CORNEAL SENSIVITY BY LOW TEMPERATURES

By

Albert Kolstad

Every person wearing contact lenses will agree that the lenses give him least discomfort in the cold season

In the summer he must gradually build up adaptation to the lenses before they can be worn all day. If they are not used daily adaptation will diminish. In the winter on the other hand he can wear lenses full time without being adapted as long as he is out in the cold. This fact is being exploited by week end skiers who are bothered by fogged eye glasses but do not have the motivation for daily use of contact lenses.

The causes for the increased tolerance at low temperatures can only be suggested

- 1 A reduction in epithelium metabolism compatible with the reduced supply of oxygen
- 2 A normalisation of an increased temperature underneath the contact lens
- 3 A reduction of corneal sensitivity

Corneal sensation has traditionally been limited to that of pain and cold. The pain sense is served by free nerve endings terminating in the corneal epithelium (von Frey 1894) while the cold sense is said to take its origin in Krause bodies located near the corneal limbus (Strughold & Karbe 1925).

The sensation of touch has more recently been added to the modalities experienced by the cornea (Nafe & Wagoner 1937, Lele & Wedell 1956) although the difference between touch and pain may only be one of stimulus intensity.

A sensation of heat is still disputed. Kenshalo and Nafe (1963) suggest that the temperature sensation originates in free nerve endings terminating on the vessel walls which in the case of the cornea would have to be the limbal vessels.

The discomfort experienced by contact lens wearers has been described as being related both to the sensation of touch, pain and heat.

function of the paralysed muscle. Resection of the paralysed muscle can in certain types also be of value. If the paralysis is almost complete, muscle transplantation can offer a good alternative. A report is given of muscle transplantations performed on 10 eyes with lateral rectus paralysis, 1 with a paralysis of the medial rectus and 3 with a paralysis of the superior rectus muscle. The results obtained were satisfactory cosmetically, and in most of the cases also functionally. Where there was fusion, the field of binocular fixation increased. Where the fusion tendency was poor or not present, the patients did not complain of any disturbing diplopia. No complications were observed after the operations.

REFERENCES

- Forbes, S. B.* Muscle transplantation for external rectus paralysis. Report of case with unusual complications. *Am J Ophth* 48, 248, (1959)
- Gifford, S. R.* Tendon transplantation for paralysis of the external rectus muscle. *Arch Ophth* 24, 916 (1940)
- Girard, L. L.* and *McNeely, R. A.* Agensis of the medial rectus muscle. *Arch Ophth* 59, 337 (1958)
- Hildreth, H. R.* The tendon transplanting operation. *Am J Ophth* 36, 1267 (1953)
- Hummelsheim, E.* Weitere Erfahrungen mit partieller Sehnenüberpflanzung an den Augenmuskeln. *Arch f Augenh* 62, 71 (1908)
- O'Connor, R.* Tendon transplantation in ocular muscle paralysis. *Am J Ophth* 18, 813, (1935)
- Spaeth, E. B.* Surgical aspects of defective abduction. *Arch Ophth* 49, 49, (1953)
- Stallard, H. B.* Eye Surgery 2nd Edition. Wright, Bristol, London (1950)
- Stucchi, C. et Bianchi, G.* Dépigmentation en secteur de l'iris consécutive à des transplantations musculaires. *Ophthalmologica* 133, 231 (1957)
- Uribe, L. E.* Muscle transplantation in ocular paralysis. *Am J Ophth* 65, 600 (1968)

mechanism Stimulus intensity is given in mg, transcribed from monofilament length using a calibration table supplied with the instrument. The esthesiometer was supported against the upper part of the lamp house. Since this was always placed on the left side of the microscope the subject was asked to look up to his right. The monofilament was then advanced perpendicularly towards the cornea midway between apex and limbus in the 12 o'clock position. Stimulation was started at the lowest stimulus intensity touching the cornea between five and ten times. If less than half the number of applications was felt the intensity was increased by shortening the monofilament by 5 mm and stimulation was repeated. The intensity level at which the subject responded to more than 50% of the stimuli was considered threshold (Villodot & Larson 1969).

Results

The following are typical values from 50 separate measurements

Ambient temperature	Corneal temperature	Sensitivity
+22 C	+32 C	12 mg
- 6	+26	7.5
-14	+24	100
-16 wind	+17	100

Discussion

Brändstrup (1952) demonstrated that a person coming in from an outside temperature of -15°C had a corneal temperature of 21° . This is a more pronounced fall than shown in table 1. This can probably be explained by the present investigation being carried out indoors where heat loss by radiation is negligible. It was always a source of surprise to enter the cold room and read the air thermometer which showed a temperature much lower than common outdoors experience would indicate. Schwartz (1965) measured 27.5°C on the rabbit cornea when room temperature was $+3.6^{\circ}\text{C}$. Other references to corneal temperature in a cold environment have not been found.

We must therefore consider the results obtained as rather conservative estimates while the actual corneal temperature outdoors may be lower.

Measurement of corneal sensitivity requires a subject sufficiently trained in the procedure to have reduced the natural reaction of anxiety to a minimum. If the examination is taking place at uncomfortably low temperatures this also reduced the availability of subjects. I have therefore performed the measurements on only two persons.

The present investigation will be limited to the sense of touch examined by the esthesiometer and subsequently termed the corneal sensitivity

Maximum sensitivity is found in the central part of the cornea, decreasing towards the periphery (Boberg Ans, 1955). A contact lens is today mostly fitted with apical clearance and touches the cornea with its periphery approximately mid-way between the corneal apex and limbus. We shall therefore concentrate our attention on the sensitivity of this area.

Methods

The two subjects investigated have normal corneal sensitivity and do not wear contact lenses. The examination took place in a cold room where the temperature could be varied between -5 and -15°C . Cooling of the cornea could be further increased by an artificial wind source with a wind speed of 5 m/sec.

The temperature of the corneal surface was measured mid way between apex and limbus in the 6 o'clock position at least five minutes after topical anesthesia with 0.4% oxybuprocaine. The measurement was performed with a Mavotherm electronic thermometer working on the principle of a thermistor placed in an unbalanced bridge. The instrument had a built in correction for change of battery voltage, and was found to calibrate with a mercury thermometer within one degree, which was the accuracy of the scale. By low ambient temperatures the glass probe accumulated a certain amount of cold, which tended to give a lower corneal reading. This could be avoided by letting the probe equilibrate with the tongue of the examiner immediately before measurement, bringing the probe into the temperature range of the cornea.

Cooling of the cornea could also be obtained without a cold room by applying solid carbon dioxide wrapped in moistened cloth on the closed eyelid, by circulating an air stream through a solid carbon dioxide-alcohol mixture and directing it against the eye or by continuously dripping Hanks solution at 4°C against the open eye. By all these means it was possible to produce corneal temperatures similar to those measured in the cold room.

The corneal sensitivity was examined on the eye which had not received local anesthesia. The subject was seated in the slit lamp, and the microscope set at 6 \times magnification. It was found advantageous to use angled oculars which allowed comfortable change between direct (unaided) and microscopic observation.

As stimulus was used a Cochet and Bonnet esthesiometer where the length of a nylon monofilament can be varied using a rack and pinion

- Midodot W and Larson W New measurements of corneal sensitivity a preliminary report, *Amer J Optom* 46 261-263 1969
- Nafe J P and Wagoner K S The insensitivity of the cornea to heat and pain derived from high temperatures *Amer J Psychol* 49 631-635 1937
- Schirmer A E Corneal sensitivity and contact lenses *Brit J Ophthalm* 47 493-495 1963
- Schwarz H Environmental temperature and the ocular temperature gradient *Arch Ophthalm* 74 231-243 1965
- Singhold H and Karbe M Die Topographie des kaltesinnes auf Cornea und Conjunctiva *Zeitschr f Biol* 83 189-200 1925

Discussion

H. Forsius (Uleaborg)

On examining Lapplanders and Eskimoes who are exposed to great extremes of climate I have often seen in elderly individuals a haziness of the epithelium at the limbus of the cornea with in extreme cases a band shaped keratitis which may lead to a partial loss of sight. It would be interesting to hear whether the sensibility of the cornea in this respect was investigated by the lecturer in connection with his low temperature studies.

A. Holstad

The limbus corneae has a higher temperature than the central part but in the case of a tear-drop collecting on the lower lid margin may reach 7°C and will then be completely anesthetic to touch. This could explain the location of epithelial damage to the inferior limbal area in cross-country skiers (Holstad and Opsahl 1969) but would probably not explain the bandshaped distribution of opacities seen in natives of the Arctic. The mechanical trauma inflicted by snow and wind would perhaps be a more likely cause.

Holstad A and Opsahl R jr Cold injury to corneal epithelium. A cause of blurred vision in cross-country skiers. *Acta Ophthalm* 47 446-453 1969

The results have been the same in both persons and in all measurements performed ■ reduction in corneal sensitivity at the temperatures commonly found outdoors in Norway during the winter. The results have been the same whether the cooling of the cornea have been caused by being in a cold room, directing a cooled air stream against the eye, dripping a cold solution on the eye, or applying a cold pack to the closed eye lid.

Is the observed reduction in sensitivity sufficient to explain that contact lenses are causing less discomfort in the winter time? Boberg Ans (1955) and Byron and Wesley (1961) have, among others, shown that adapted contact lens wearers have a moderate hypoesthesia of a similar magnitude. It has also been shown that persons who have not been able to adapt to contact lenses because of discomfort have a sensitivity which is higher than normal (Schirmer, 1963).

Recent work by Feldman, Flanary, Bruechert and Sampson (1969) has seriously challenged the theory that adaptation to contact lenses is explained by an increased tolerance to hypoxia. We may therefore have to look for other theories. A reduction in corneal sensitivity is certainly a nice theory, if for no other reasons than its simplicity. As an explanation of the increased tolerance to lenses during the winter it may even be the right one.

Summary

Exposure to ambient temperatures common in Norway during the winter is found to decrease the corneal sensitivity as measured by an esthesiometer. It is thought that this may explain the higher tolerance to contact lenses experienced during the cold season.

REFERENCES

- Boberg Ans, J. Experience in clinical examination of corneal sensitivity. *Brit J Ophthal* 39: 705-726 1955.
- Brandstrup J. M. Ojets kliniske temperatur p 60 Copenhagen 1952.
- Byron H. M. and Wesley A. C. Clinical investigation of corneal contact lenses. *Amer J Ophthal* 51: 675-694 1961.
- Feldman G. L. Flanary L. M. Bruechert R. W. Sampson W. G. New concepts in corneal adaptation to contact lenses. *Contact Lens Medical Bulletin* 2: 8-10 1969.
- von Frey M. Beitrage zur Physiologie des Schmerzsinnes. *Ber Sachs Ges Wiss Leipzig* 46: 185 1894.
- Kenshalo D. R. and Aafe J. P. The peripheral basis of temperature sensitivity in man. In: *Temperature its control and measurement* edit J Hardy p 231-238 vol 3 New York 1963.
- Lele P. P. and Wedell G. The relationship between neuro histology and corneal sensibility. *Brain* 79: 119-154 1956.



Fig 1

Wheel like formation with radiate folding of the macula in a case of X-chromosomal retinoschisis

pigmentation (Fig 10) In the schisis area the retinal function is reduced which results in more or less pronounced visual field defects According to some investigators these defects correspond to the extension of the process while others maintain that some function remains in the area involved

Our studies on X chromosomal retinoschisis started in 1962 with the description of a family with this disease (Forsius *et al* 1962) Up to now we have collected 170 cases of retinoschisis varying in degree It may be mentioned that our series includes the only homozygous female case described in the literature and a four month old boy with severe retinoschisis (Fig 2)

The present paper is a preliminary report on the findings in 29 patients with X chromosomal retinoschisis investigated by fluorescein angiography (Novotny and Alvis 1961)

On the basis of the clinical findings the series may be classified as follows

- 1 Mild cases showing only macular involvement
- 2 Moderate cases showing schisis or veils with retinal holes peripherally in addition to a typical macular finding

FLUORESCEIN ANGIOGRAPHIC STUDIES ON X-CHROMOSOMAL RETINOSCHISIS

By

*U Krause, Birgitta Vainio Mattila,
A Eriksson and H Forsius*

As a clinical entity juvenile retinoschisis was described for the first time in 1932 by both Thomson and Andersson Sorsby, in 1951, found that the disease is recessively inherited via the X-chromosome. This has later been confirmed in several investigations (e.g. Vainio Mattila *et al* 1969). As regards the histology of the disease, it was assumed that splitting of the retina in the ganglion cell layer is involved (Levy 1952, François *et al* 1963). This theory was conclusively proved correct in 1968, by Yanoff *et al*, who studied an enucleated eye. The histological difference between X-chromosomal retinoschisis and autosomal hyaloid retinal degeneration described by Bohringer *et al* (1960) is thus clear. Amalric (1968) investigated angiographically a case of retinoschisis without discussing the heredity. His findings were indicative of markedly dystrophic changes in the choroid. Using the same technique, Lemke, Jutte and Scheibe (1968) clearly demonstrated the presence of vascular veils. The relevant literature has recently been surveyed by Bengtsson and Linder (1967).

The pathological process is sometimes limited to the macula, which in young patients shows a wheel-like formation with radiate folding (Fig 1), due to cystic degeneration of the innermost retinal layer. Independently of the macular process, peripherally or nearer the papilla the elevated inner retinal layer may form a veil extending towards the vitreous, as a rule temporally below. The findings in the two eyes are often, though not invariably, symmetrical. In some cases the veil forms a roll towards the vitreous (Fig 10). Sheathing of retinal vessels is frequently seen peripherally and round the papilla, and haemorrhages have been observed (Bengtsson and Linder 1967). These may also involve the vitreous. Anomalies of the papilla, e.g. in the form of pseudopapillitis, optic atrophy and drusen, have been described by many authors (Levy 1952, Forsius *et al* 1962). The choroid exhibits various degrees of degeneration (Sorsby 1951, Forsius *et al* 1962, 1963) and sclerosis, associated with changes in



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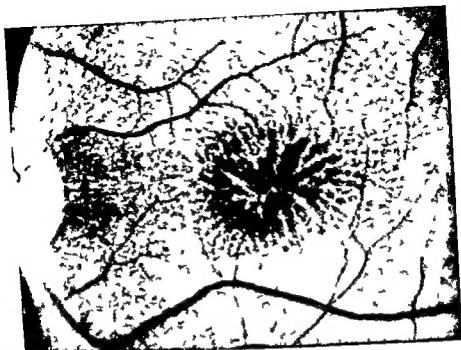


Fig 1

Wheel like formation with radiate folding of the macula in a case of λ chromosomal retinoschisis

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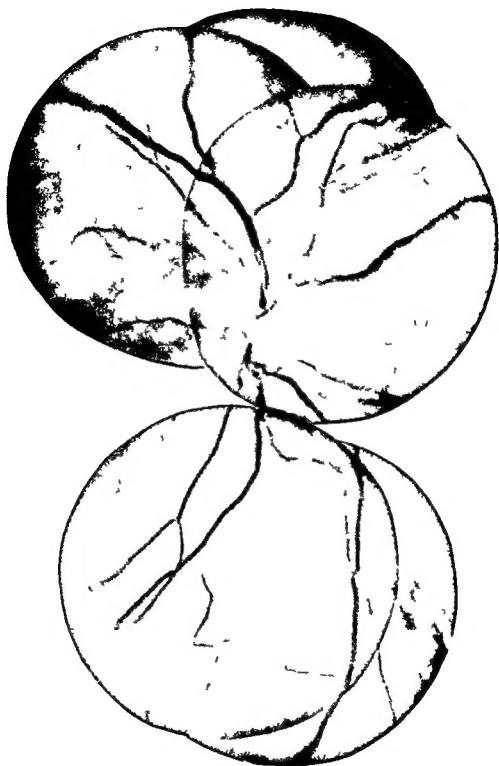


Fig 2

Severe retinoschisis in a boy aged 4 months. Only a small sector of the retina (from 8 o'clock to 10 o'clock) is intact

- 3 Severe cases showing schisis extending to the vicinity of the papilla and/or other severe anomalies involving the papilla, vessels or vitreous

We have come to the conclusion that as defined above, or in other words in regard to type or form, the disease remains the same throughout life, although within the above mentioned groups the course is slowly progressive so that probably all patients finally lose word vision

In general ordinary black white photography reveals the pathological changes in the macula more clearly than colour photography or even ophthalmoscopy in red free light

In Fig 3A (case 1) the slightest macular changes in the series may be studied There is only a suggestion of a wheel like formation This patient has a visual acuity of 0.5 The angiogram (Fig 3B) shows an intact pigment epithelium in the macular region, without fluorescent areas The next ordinary black white photograph (case 2, Fig 4A) shows a definite wheel like formation in the macula and perimacular radiate streaks As compared to the first case (Fig 3A), the process is more advanced but nonetheless the patient has a visual acuity of 1.0 The angiogram (Fig 4B) displays a normal macula but nasally there is a certain patchiness due to slight atrophy of the retinal pigment epithelial layer

Patient No. 3 has a visual acuity of 0.7 The ordinary black white photograph (Fig 5A) shows a patchy macula with a slight indication of a wheel like formation and perimacular radiate folding in the retina The macular pigment epithelium is in part destroyed and the underlying fluorescent choroid shows through (Fig 5B) In all other cases in our series destruction of the pigment epithelium is associated with a visual acuity under 0.1

In case 4 vision is finger counting 4.5 m The ordinary black white photograph (Fig 6A) reveals coarsely granular destruction in the macular region and in the angiogram (Fig 6B) the depigmented areas show clearly through The next series of pictures (case 5) demonstrates the purely macular process in a 68 year old patient whose vision is finger counting 3.5 m On the ordinary black white photograph (Fig 7A) a localized process is seen, with pigment spots in the macula and tortuous light zones which seem to extend outside the macular region At the beginning of the arterial phase (Fig 7B) a fluorescent ring is discernible round the macula and the light areas appearing on the black white photograph are more conspicuous temporally Five seconds later the fluorescence of the nasal areas predominates (Fig 7C) At this point it is difficult to interpret the angiographic finding These pictures show the